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CERTAIN NEW OBSERVATIONS ON THE ACTION OF THE ANTERIOR PITUITARY*

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AT THE present writing there is no doubt that the anterior lobe of the pituitary gland promotes the growth of follicles and thereby the production of the female sex hormone in the ovary. This knowledge is the result of the investigations of Long and Evans, Smith and Engle, Zondek and Aschheim. These authors showed that the implantation of anterior pituitary substance induces the maturation of follicles, while administration of its extract causes luteinization. Whether the antagonistic effects upon the ovaries of immature animals are due to two different hormones, or to varying quantities of a single hormone, is not quite clear. Nevertheless the majority of these authors hold the first point of view: Evans and Long distinguishing a sex hormone and a growth hormone, Zondek and Aschheim a prolactin A and B, and Crew and Wiesner a rho I and a rho II. However, these several substances were produced as chemical extracts by rather complicated methods, while little attention was paid to the fact that the implantation of pure hypophyseal tissue might also produce similar effects.

We already know that the anterior lobe of the pituitary may be influenced by many factors, mainly in connection with the sex organs. Erdheim and Stumme have described the typical changes in pregnancy, and Fischera, Luziani, Marassani those following castration and occurring during menopause. Berblinger, Adachi, Lehmann, Baniecki have shown that both placental substance and ovarian hor-

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mone cause histologic alterations in the anterior pituitary quite similar to those in pregnancy. Furthermore that after castration, the gland can be restored to its former state by administration of folliculin. Asehheim and Zondek drew attention to the tremendous increase of anterior pituitary hormone in the blood, as well as in the urine, just after the onset of the pregnancy, and particularly in cases of hydatidiform mole and chorionepithelioma. B. Zondek also demonstrated that great quantities of prolactin A were secreted in the urine after castration or early in the menopause. The same occurs in connection with malignant tumors, chiefly of the generative system, and as reported by MacCallum and Fabyan, Schilder, Schultze and Zuckermann, pregnancy-like changes in the tissue of the anterior pituitary in the thyroplasia. On the other hand, Wagner has reported a case of a tumor in the anterior pituitary associated with tremendous luteinization of both ovaries. Berblinger found that he could produce changes in the anterior pituitary like those of pregnancy by peptone injections, and Baniecki made similar observations after the injection of the urine of pregnant women and of horse serum. Therefore Berblinger, as well as Karlefoss and Muth, consider that changes noted in the anterior pituitary in malignancy and pregnancy are due to protein bodies. H. Zondek has formulated a so-called "periphery theory," and believes that any bodily event may influence the entire organism, even the hypophysis. This, indeed, is quite probable, in the light of what we know concerning the mutual interaction of the endocrine tissues of the organism.

According to Evans and Simpson the anterior pituitary of gonadectomized animals has been found more effective than in normal animals. Following the same authors, the male gland shows an increased potency in comparison with the female. Furthermore, they could not find an increased action of the anterior pituitary of pregnant animals. Finally the same authors state exactly that the implantation of hypophyseal tissue is more effective than the injection of an extract, made of the urine of pregnant women.

Methods.—In view of the above findings, we desired to ascertain, if possible, by biologic assay, whether or not there are any differences in the effects of implanted anterior pituitary glands which had been exposed, before transplantation, to any of the following conditions: (A) Daily administration of placental tissue, as well as to extracts made from it. (B) To corpus luteum extract. (C) To folliculin. (D) To urine from pregnant women. (E) Finally to adrenalin injections. We wished to learn the effect of the pituitary gland removed from animals after operative or x-ray castration, as compared to the effect of the irradiated gland. I desired to see the effect of the anterior pituitary of pregnant animals as compared with nonpregnant ones, particularly because E. Philipp had reported that he obtained negative results in

immature mice with implantation of hypophyses taken from women during or immediately after gestation. I used immature mice fourteen to twenty-four days old for the tests, litter-mate animals being used as controls. Though I intended to investigate only the qualitative differences in the effect on the ovary, I noted quantitative differences as well. The whole gland was employed throughout my experiments, since by including the posterior portion, I felt, that I would introduce less error than by the loss of substance incident to dissecting out the anterior lobe.

Results.—In group A the implants were taken from four rabbits which had received daily injections of placental extract over a period of six days. My extract was prepared from human placenta at term by the alcohol, ether, and acetone method of Corner. I found that

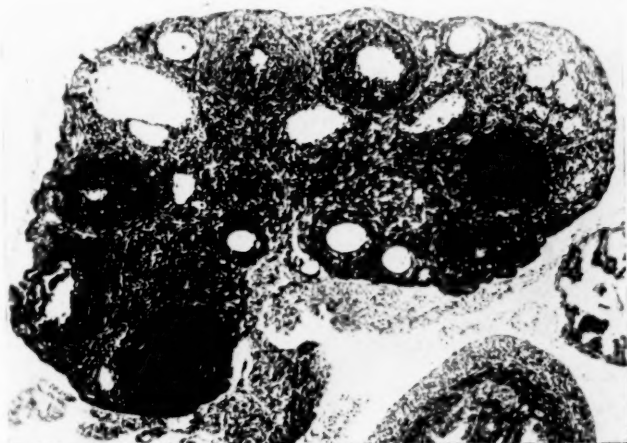


Fig. 1.—Ovary of mouse, three weeks old, six days after implantation of anterior pituitary of a female rabbit previously injected with placental extract.

such implants produced changes in the ovaries of immature mice considerably different from those described by Smith and Engle, who used normal glands. In my experiments the ovaries showed an increase in size and weight, a preponderance of lutein tissue and many pseudocorpora atretica. The granulosa lutein cells completely filled the lumina of the follicles and imprisoned the degenerating ova. On the other hand some of the follicles showed an unmistakable tendency toward development. The ovaries were quite congested as evidenced by enlarged and engorged capillaries, while an occasional hemorrhage was seen in the stroma outside the vessels proper. The vaginal smear rarely showed cornified cells exclusively, but rather a mixture of cornified and nucleated epithelial cells.

I used Corner's method for extracting the placenta, particularly to determine if this tissue contains corpus luteum hormone, as it is gen-

erally conceded that the placenta assumes the function of the yellow body after the latter degenerates. I injected this extract into female rabbits, which had previously been ovariectomized, eighteen hours after copulation, and in their uteri five days later I could find no growth of the mucous membrane; from which it may be deduced that the human placenta at term contains no corpus luteum hormone. On the contrary, the extract has been found to contain large amounts of folliculin, as tested on both castrated and immature mice. I shall make further reference to the effect of folliculin on ovaries of mature animals in connection with studies upon the corpus luteum hormone and the urine of pregnancy.

In the placental implantations I inserted the whole placental disc of guinea pigs and rats under the fascia in the backs of four rabbits,

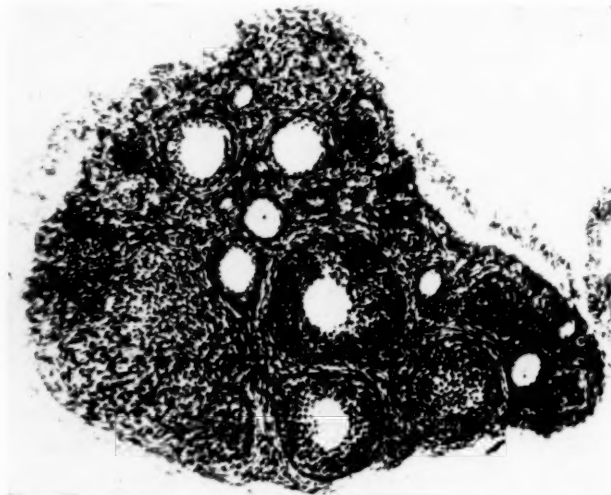


Fig. 2.—Ovary of three weeks' mouse, six days after implantation of one pituitary gland of a female rabbit previously implanted with five discs of guinea pig placenta.

making five such implantations in two weeks. At the end of that time the hypophysis of the rabbits was removed and placed in the thigh muscles of immature mice, which were killed six days later. Their ovaries showed a high degree of development, and the vaginal smear disclosed only cornified epithelium. On section, the ovaries contained one or several mature graafian follicles at the point of rupture, and their development seemed more pronounced than in animals treated with glands prepared by an extract of human placenta. In this connection one must take into consideration the fact that the placenta of the guinea pig and rat has been found to be relatively poor in folliculin, and that the implantation of placental tissue introduces the factor of parenteral protein effect. While some of the follicles are undergoing a cystic change, several pseudocorpora are to be found in

the ovaries. Finally, the effect of the anterior pituitary seems to be increased by the placental implants. Both the follicular maturation and the luteinization are increased simultaneously, but neither appears to be predominant. This is in contrast with the result obtained after implantations of gland prepared by placental extract. The latter causes chiefly, as mentioned above, luteinization, whereas the gland prepared by the whole placenta seems to yield an increase of both anterior lobe principles.

In group B I extracted yellow bodies of pigs by Corner's method with alcohol, ether, and acetone, and the extract so prepared appeared to have the same properties as one kindly sent me by Dr. Corner. In this series of experiments, I sometimes implanted fresh corpus luteum tissue directly, and at other times I injected the extract into three

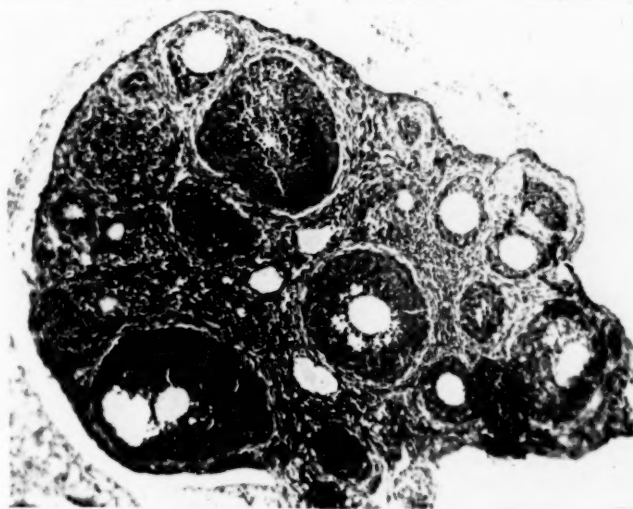


Fig. 3.—Ovary of mouse, three weeks old, six days after implantation of three pituitaries of adult mice previously injected with corpus luteum hormone.

rabbits, five guinea pigs, five rats, and six mice over varying periods. The hypophyses of these animals were then implanted into immature mice. The ovaries of the latter showed a definite stimulation of lutein tissue; many pseudocorpora filled the tiny ovaries, which were really smaller than the average immature ovary stimulated by anterior pituitary implants. The development of follicles is not completely inhibited, but it is distinctly diminished. The vaginal smear has never shown signs of estrus, only cornified cells mixed with leucocytes and nucleated epithelial cells being formed.

In group C I prepared the hypophyses of three rabbits, five guinea pigs, and six mice by injections of "Amniotin, Squibb," containing female sex hormone. These hypophyses were then implanted into immature mice, whose ovaries became quite mature after six days. They

show large graafian follicles alternating with great pseudocorpora in about equal numbers. The ovaries are very congested, but there is no hemorrhage in the interior of the follicles. The changes resemble those produced by the pituitaries of animals treated with placental tissue (group A). In other words, a marked anterior pituitary effect is observed in both its phases, namely, maturation and luteinization of follicles. The number of follicles undergoing luteinization is evidently greater than after implantation of a normal anterior pituitary body.

In group D we used the pituitary glands of five rabbits and six guinea pigs which had been injected with urine from women in the various months of pregnancy and during the puerperal state. Some of the animals received daily injections of two to five c.c. over a period

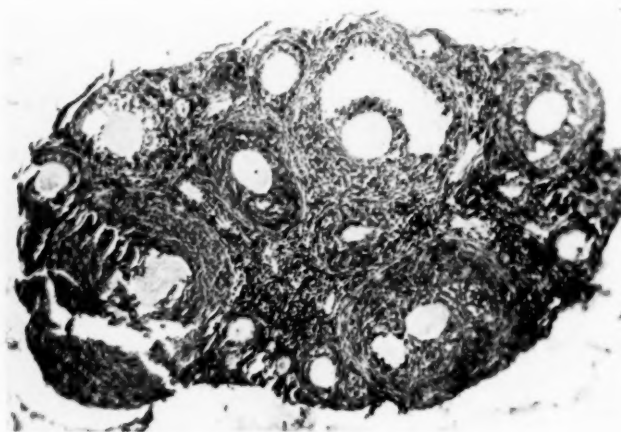


Fig. 4.—Ovary of three weeks' mouse, six days after implantation of three pituitaries of adult mice previously injected with Amniotin, Squibb.

of four weeks. Naturally they lost weight. On examination the mice ovaries showed a decided increase in lutein tissue, but in many cases it was impossible to decide, whether the maturing or the luteinizing effect was in the ascendancy, as both were much in evidence. However, I can say that there are more pseudocorpora, a thicker granulosa layer in the graafian follicles, and a rather more compact than cystic appearance as compared with the ovaries of mice six days after implantation of normal pituitaries. No clear difference could be demonstrated between the action of urine from different stages of pregnancy, nor between it and that from puerperal women. I also injected such urine into a rabbit four weeks after oöphorectomy and its anterior pituitary similarly produced highly luteinized ovaries.

In group E three normal female rabbits were injected with one or two mg. of suprarenin daily for two weeks. Their pituitary was then implanted into immature mice. The ovaries showed a general de-

velopment of follicles up to the graafian stage, but no luteinization. It seems rather remarkable that while such an anterior pituitary has no luteinizing effect in the mice, the ovaries of the donor animals showed tremendous luteinization.

The aspect of the rabbit ovaries is that of a single great interstitial gland with a few degenerating follicles. (I drew attention to this

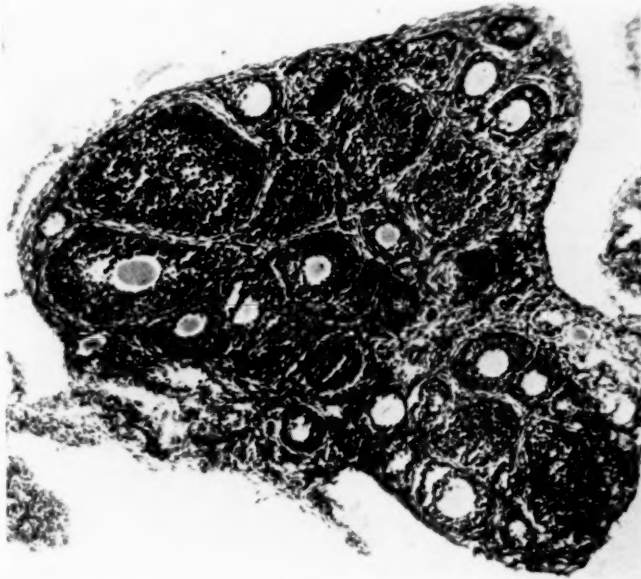


Fig. 5.—Ovary of mouse, three weeks old, six days after implantation of one rabbit pituitary, previously prepared with urine of pregnant women.

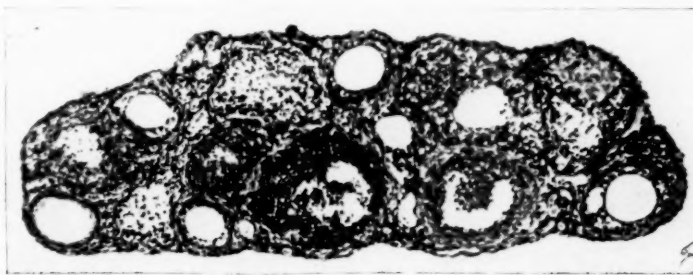


Fig. 6.—Ovary of twenty-one day mouse, six days after implantation of a rabbit gland previously prepared with suprarenin.

luteinizing effect of suprarenin some years ago.) One of the rabbits injected with suprarenin was pregnant and aborted three days after the first injection. The interaction of ovary and adrenal is not yet clear, but it offers much promise for further investigation.

At this point I shall revert to my castration experiments: In the first group were used hypophyses of three guinea pigs, which had been sterilized six weeks previously by an intensive x-ray irradiation of the

abdomen. The glands from them produced a striking luteinization in the ovaries of infantile mice, characterized by a large number of pseudocorpora lutea with relatively few graafian follicles. In the donor pigs there was a complete absence of vaginal cycle, the vagina itself failed to open, and the ovaries were atrophic, presenting a diffuse fibrosis through which were scattered a few cystic, completely degenerated follicles, entirely free from lutein tissue. This observation is rather interesting in the light of the findings in the ovaries of the donor animals in the suprarenin group.

Though it is not within the scope of this paper, I should like to call attention briefly to the effect of irradiation upon the ovary. In my studies rabbits, guinea pigs, and mice received a large dose of x-rays,

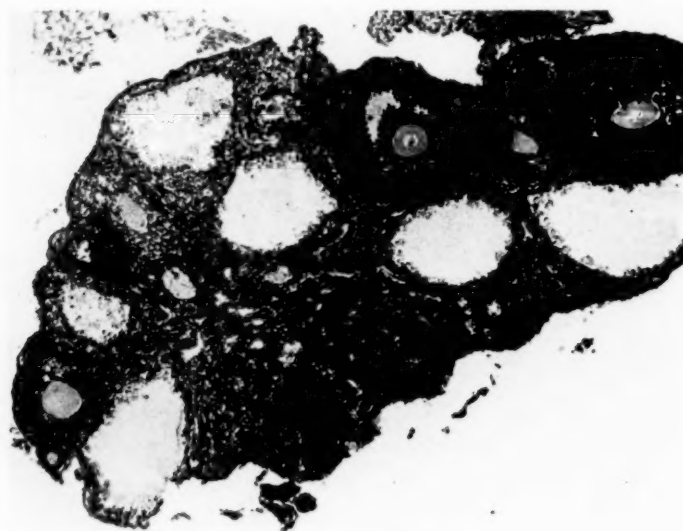


Fig. 7.—Ovary of twenty-two day mouse, six days after the implantation of one pituitary gland of a rabbit irradiated six weeks previously.

namely, 20 per cent of the human erythema dose, with an intensive apparatus. Six weeks following such an exposure, one finds extensive fibrosis of the ovaries, as mentioned above. With smaller doses persistent corpora lutea, signs of regeneration, and a normal vaginal cycle, occasionally going over into continuous estrus are noted, first described by Parkes and Bellerby, von Schubert, Geller and others.

Irradiation of the head alone is followed by sterility, due to the changes in the ovaries, consisting in diffuse fibrosis interspersed with degenerated middle-sized and primary follicles.

Implantation of irradiated hypophyses produces a nearly normal effect on the immature mouse ovary, namely, follicular maturation without stimulation of the lutein elements, though in one case it was increased.

When irradiation was supplemented by a placental implant some weeks later, the hypophysis from this animal produced many pseudo-corpora in the ovaries of immature mice (cf. group A). In a second series of experiments, I used anterior pituitary taken from rabbits and guinea pigs four to six weeks after oöphorectomy, with the following results: Principally an extensive luteinization, paralleled by a similar degree of follicular maturation. It may also be added that the

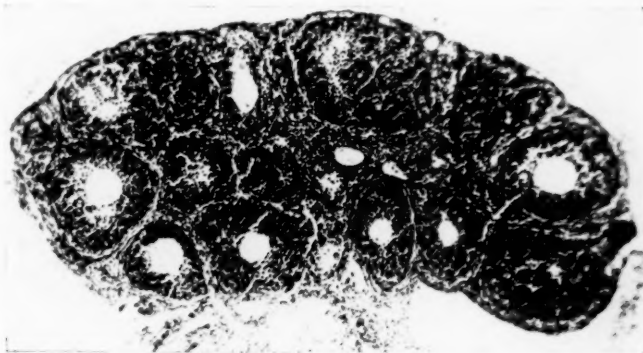


Fig. 8.—Ovary of twenty-six day mouse seven days after the implantation of pituitaries of pregnant guinea pigs; one each was implanted on three successive days.

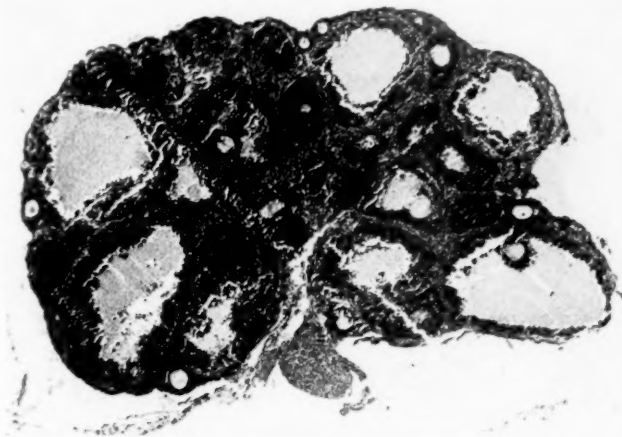


Fig. 9.—Ovary of twenty-one day mouse, six days after the implantation of a pituitary of a normal, female rabbit.

anterior pituitary of the ox caused an even more striking luteinization of the immature ovary. Since B. Zondek had pointed out that after castration, and in the early menopause, the urine contains large amounts of prolan A (the follicle promoting principle) I was rather surprised at this result.

I further interested myself in the effect of pregnancy upon the implanted hypophysis, as reflected by the activity of the latter in the implanted animal. I used, with the exception of one cat, the hypoph-

yses of 20 guinea pigs. I had rather expected an increased effect, since it is known that in pregnancy the hypophysis enlarges, that the blood level of its hormone is raised, and that there is a tremendously increased output in the urine, but I was surprised to find quite the contrary. While the ovaries showed some follicular growth, it was very

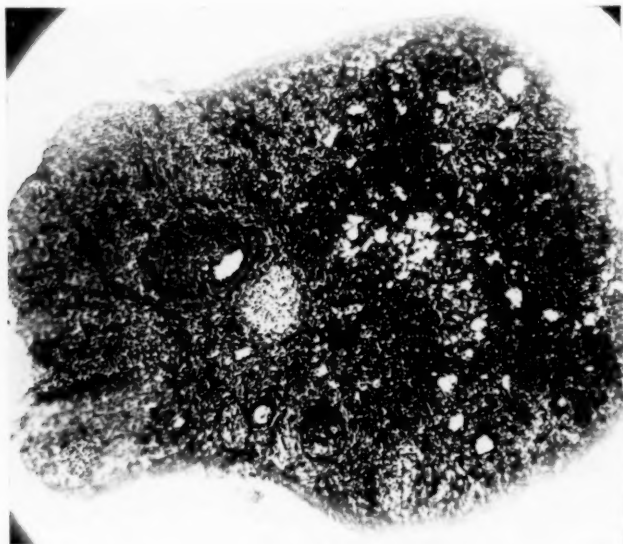


Fig. 10.—Ovary of adult mouse following corpus luteum hormone injections.

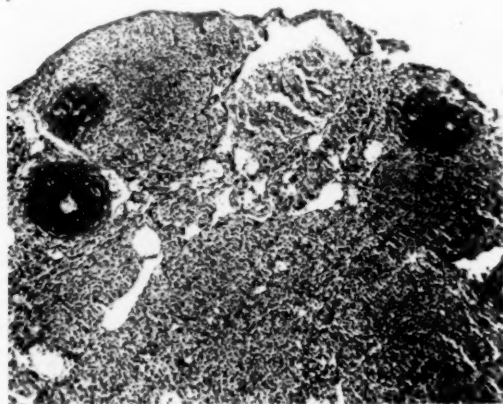


Fig. 11.—Ovary of adult mouse after injections of urine of pregnant women.

much less than I had expected, whereas the luteinization was definitely increased. Furthermore, I found that I could not produce frank follicular growth unless two or three anterior pituitary bodies from pregnant guinea pigs were implanted, whereas the implantation of one or two glands from nonpregnant animals would produce a distinct effect. The reverse is apparently true as regards luteinization, since one-half

the cat gland was sufficient to cause follicular maturation and luteinization. I reserve for later discussion the apparent discrepancy between our prediction and actual observation.

DISCUSSION

When one compares the findings in the ovaries described above, with those produced by the normal hypophysis, there is an unmistakable difference. The results from normal implants are well known from the work of Zondek and Aschheim, and Smith and Engle, and the great development of follicles in all stages of maturation up to the point of superovulation has been confirmed many times.

On the other hand, it is a fact, until recently neglected, that the implantation of normal pituitaries may also produce an inconstant picture, varying from a scarcely perceptible to an unmistakable degree of luteinization. To a certain extent, this mixture of growing and degenerating follicles associated with more or less luteinization of the granulosa layer or of the theca, is a physiologic occurrence. However, in my experiments the ovaries, as compared with those of normal immature and normal-gland-implanted mice, show a distinct increase in lutein tissue.

We find that it is necessary to distinguish two distinct and entirely different actions of the anterior lobe: one, stimulating, follicular growth, and the other producing luteinization. This, I believe, speaks for the existence of two corresponding hormones in the anterior pituitary which act simultaneously upon the ovary. These two principles are essentially antagonistic in their effect, though the one does not necessarily inhibit the activity of the other. By this, I mean that stimulation of the luteinizing hormone by placenta, for instance, has very little effect upon the activity of the follicle-promoting principle, whereas, on the other hand, in highly luteinized ovaries of young mice there are many evidences of follicular growth. I do not infer that such an equilibrium exists, and that a reduced amount of the one principle causes a relative hyperactivity of the other, yet I cannot but feel that the automatic interaction of both ovary-affecting hormones is somewhat analogous to the automatic balance between the sympathetic and parasympathetic nervous systems, as manifested in the vegetative processes elsewhere in the body.

It may be that the maturation-principle is usually more easily liberated from the implanted tissue than the luteinizing hormone, as suggested by Evans and Long. However, under certain conditions, such as those produced above in our experiments, the luteinizing principle apparently becomes more active. When the problem is attacked from the chemical angle, a similar conclusion has been reached, and Crew and Wiesner, as well as Zavadowsky, have isolated two prin-

ciples from the anterior pituitary, one of which induces ovulation and the production of folliculin (estrin), and the other, the activation of lutein tissue.

From such artificial procedures as obtained in our experiments, one cannot, without reservation, transfer one's observations and conclusions to the physiologic activity of the gland in situ. Contrary to what was once thought, excessive amounts of the maturation-principle do not necessarily produce luteinization. In such experiments we occasionally find small ovaries with an appreciable luteinization on the one hand, while on the other, a tremendous growth of follicles even approaching cystic degeneration, without any demonstrable luteinization.

Placental Implants in Immature Mice.—Since it was shown by Murata and Adachi, Zondek and Aschheim, and E. Philipp, that human placental tissue, principally from the early months of pregnancy, promotes the maturation of infant animals, I implanted the placentae of rabbits, guinea pigs, rats and a cat, in order to compare their effects with those of the human placenta. My findings confirm those of the other investigators, even to the follicular maturation and the formation of pseudocorpora. However, the animal placentae do not appear to be so potent in producing such effects as the human. We cannot, from our experiments, throw any new light on the problem of the storage or production of this hormone in the placenta; although the lesser effect of animal placentae is in line with the observation that the urine of pregnant animals (except in primate monkeys) has no effect upon immature mice, and gives a negative Zondek-Aschheim test.

The Zondek-Aschheim Effect.—I should like to direct attention to some of my observations upon the effect of the urine of pregnant women upon immature mice. As is well known, follicular growth, luteinization, and follicular hemorrhage (so-called "blood spots"), follow injections of such urine, and is the foundation for the most efficient pregnancy test we have. Though the practical value of the Zondek-Aschheim test is undoubted, its mechanism is not yet clear. Are the large quantities of luteinizing substance, found in the urine of pregnant women, and to an even greater extent in those presenting hydatidiform mole or chorionepithelioma, produced by the placenta or by the pituitary gland? Is its excretion by the kidney due to a spilling-over of an excess in the blood stream, or does it result from an increased filtration incident to a lowered renal threshold, as is noted in pregnancy for such substances as glucose, lactose, etc.? This follows the suggestion of R. Frank for cases of so-called hyperhormonal amenorrheas. We already know the connection between the posterior pituitary and renal secretion, and need only to suggest a somewhat analogous process for the anterior lobe.

The Zondek-Aschheim findings are probably brought about by several substances in the urine of pregnant women. This contains large amounts of folliculin, as does the placenta, which apparently produces it. This folliculin is perhaps the agent active in producing the blood spots characteristic of the Zondek-Aschheim picture, since I noted a similar phenomenon on its injection into adult mice. In addition, such urine also contains small amounts of follicle stimulating hormone, probably of anterior lobe origin, as well as a luteinizing principle, possibly derived from the same source. One cannot definitely exclude the possibility that the placenta may produce the latter substance. We have seen above that if one injects urine of pregnant women into animals, the anterior pituitary is stimulated and is manifested by luteinizing the ovaries. In the Zondek-Aschheim effect luteinization preponderates likewise. Therefore the mechanism of the Zondek-Aschheim effect includes at least two possibilities: (1) the hormone content of the urine itself, and (2) the stimulation of the anterior pituitary gland of the test animal by the urine, together with the resultant increase in hormone from this action. The question, as to which of these processes is the more potent, cannot be answered without further experimentation, principally by means of hypophysectomized animals. I am now engaged with C. Bernstein Jr., H. S. Schiro, and W. J. Turner, in such experiments, and we hope to publish our results in the near future.

It would be well to recall here that Aschner, Fellner, Schickelé, Frank and Rosenbloom, as well as Allen and Doisy, even before the discovery of the anterior pituitary action on ovaries, described production of premature puberty in animals by placental and ovarian hormone. As indicated above, I have observed in infant mice, treated with daily injections of "Amniotin, Squibb," an increase in growth over litter-mate controls, as well as the fact that the ovaries are larger and show many pseudocorpora.

Other Experiments.—It seemed not without promise to investigate the action of various other endocrine substances on the normal ovary, including corpus luteum extract, folliculin, placental extract, and urine of pregnancy.

Corpus luteum extract or implantation causes varying degrees of luteinization, in direct proportion to the quantity used. The changes vary from a slight alteration of follicular growth with very small amounts of extract to a complete suppression of ovarian activity with larger amounts.

Folliculin (Amniotin, Squibb) seldom completely suppresses the ovarian cycle, unless doses approaching toxic levels are used. Blood spots are, however, a frequent finding.

Placental extract acts much the same as corpus luteum, always permitting of some follicular growth.

Urine of pregnant women produces a luteinization and hyperemia, and occasionally typical follicular hematomas. Small amounts change but little the follicular maturation, and leave the vaginal smear unaltered, whereas large doses completely suppress follicle-growth and lead to continuous estrus in the sex cycle, no doubt due to the large folliculin content.

While producing the changes just described in the ovary, all of these substances may at the same time be acting on the anterior pituitary. What is the direct, and what the indirect effect, cannot be decided except by hypophysectomy experiments. The possibility that such changes occur first in the ovary and then in the hypophysis, or vice versa, is another problem, which we hope to attack later.

In this report the term "luteinization" has been used so often, that I wish to clarify my conception of the term. I do not mean by it the physiologic formation of a normal yellow body, but rather the well-known changes that sometimes occur in unruptured follicles as evidenced by enlargement of the granulosa and theca interna cells, by an increase in the thickness of the follicular wall, and by the ramification of the capillaries. Such a follicle is a pseudocorpus luteum, and imprisoned between its hyperplastic lutein cells, one frequently finds the degenerated ovum. Physiologically in pregnancy, one finds occasionally the walls of the medium-sized follicles undergoing luteinization. These changes are accentuated to the point of cyst formation in hydatidiform mole and chorionepithelioma. The same change which produces normal luteinization in ruptured follicles results in the formation of pseudocorpora from unruptured follicles. The ovaries of many animals, especially the rodents and more particularly the rabbit (with its nonspontaneous ovulation), show large areas of extrafollicular lutein tissue, the so-called interstitial gland. The entire question of the interstitial gland, of the differences between pseudocorpora and normal follicular degeneration is too well worked out in the literature to call for extended discussion here.

Here I should like to mention the statement of P. E. Smith and E. T. Engle that the coincidental stimulation of both follicular growth and luteinization may produce so-called intermediate bodies, which are characterized as hybrid structures between follicles and corpora.

I was interested to learn whether pseudocorpora contain hormone of any importance in the physiologic economy. We know from Fraenkel's and recently from Corner's investigations, that the corpus luteum produces its own hormone, which acts on the uterine mucous membrane, on the myometrium, etc. In order to determine the presence of a corresponding hormone for the pseudocorpus, I implanted luteinized ovaries into ovariectomized rabbits twenty hours following sterile copulation. These ovaries had been made rich in interstitial glandular tissue by previous placental implantation in the donor ani-

mal. Five days later the uterine mucous membrane showed a distinct hyperplasia, indistinguishable from a true corpus luteum effect. This, I take it, signifies that the pseudocorpus produces an active, corpus luteum-like hormone.

There is no doubt that the normal yellow body has a certain degree of independence. This is in accordance with the observations of Westmann who, after excising the fallopian tube and uterine horns from rabbits following sterile copulation, succeeded in showing that although ova had been removed, the corpus luteum retained its functions as proved by the progressive hyperplasia of the uterine mucosa. I have repeated such experiments in five rabbits, properly controlled with unoperated animals, and have confirmed Westmann's results.

P. E. Smith stated that the corpora lutea persist for several weeks after hypophysectomy, in spite of the retrogression of the other ovarian tissue, and I have been able also to confirm his observations. On the other hand, Teel showed that an alkaline extract of the anterior pituitary stimulates the corpus luteum, and by its use was able to prolong pregnancy in animals from two to six days past term. At the same time one should constantly bear in mind that in the human the ovary has not nearly the same tendency toward luteinization as in rodents, and particularly in the rabbit.

It is well known that the placenta is intimately linked up with the process of luteinization, for as long as placental tissue remains in the organism large amounts of a luteinizing substance can be obtained from the urine. Whether it is produced by the placenta itself, or results from stimulation of the anterior pituitary by the latter, we hope to determine in hypophysectomized rats. This increase in the luteinizing substance is apparently of great importance in inhibiting superfluous ovulation during the period of gestation, following degeneration of the yellow body. In rodents the yellow body persists throughout the course of pregnancy, although their placentae do not contain such great amounts of hormone as the human being, and their blood serum shows no increase of anterior pituitary hormone during pregnancy. An exception apparently exists in the case of the mare, whose blood serum contains high amounts (Cole and Hart). In this animal, however, the yellow body degenerates before the termination of pregnancy.

Both folliculin and corpus hormone act on the uterine mucosa, on the mammary gland, and on the anterior pituitary partly synergistically and partly antagonistically. The corpus luteum hormone, as shown, requires the previous action of folliculin, but excess of the latter inhibits the action of the former. The pituitary gland apparently has a regulatory function in the quantitative relationship of the hormones, which is very important, as an excess of anterior lobe principle prevents normal estrus, as shown by the investigations of Smith

and Engle. Furthermore Hofbauer has succeeded in producing in guinea pigs a condition simulating hyperplastic endometritis by an excess of anterior pituitary extract. Another example of the importance of this hormonal equilibrium is the observation that an excess of folliculin, as well as of corpus principle may cause abortion, although both are necessary for the normal course of pregnancy.

Some of the endocrine glands have the ability to store hormones, for example, the human yellow body in pregnancy contains folliculin as well as anterior pituitary hormone. The placenta also contains several hormones. Therefore I was interested to know whether the anterior pituitary stores them similarly. After injections of folliculin for a week, the anterior pituitary of adult mice was implanted into castrated mice, and as they showed no estrual signs, it may be concluded that the anterior pituitary does not store folliculin.

COMMENT

There is no other branch of medical research in which one treads on thinner ice than in the field of endocrinology. Consequently one must exert the greatest care to avoid the invention of attractive hypotheses. However, the observations concerning the various effects of pituitary tissue described in this report, provoke the inevitable question: Do they throw any new light on the physiology of the anterior pituitary gland in its relation to the sex cycle? Does the ovarian cycle respond to a "pituitary rhythm"?

We know that the anterior pituitary promotes follicular growth; that the latter is inhibited by the corpus luteum. Does the inhibitory action of the latter on the ovaries bear any relation to the pituitary, and if so, what, and how is it brought about? Is it due to inhibiting the activity of the follicle-promoting hormone, or to increasing the lutein-promoting principle? At this time these questions cannot be answered definitely. Notwithstanding these reservations, I feel justified in concluding from my observations that the resorption of the follicular fluid and its principle, as well as the corpus hormone (the placental hormone also), all exert an important, qualitative and quantitative influence on the pituitary gland. The anterior pituitary has been called the "motor" of the ovary. I should call it, in addition, the "regulator."

Among the stimulating effects of the anterior pituitary on the ovary are to be distinguished the promotion of follicular development, and the production of the so-called female sex hormone (folliculin). That these are not entirely parallel functions is evidenced by the fact that the latter is found in many places outside the ovary, chiefly in the placenta, as well as shown by the work of R. Frank, who found that the crest of blood folliculin does not coincide with the rupture of the

graafian follicle. In the ovary as in other organs, its momentary state is of the utmost importance, particularly in its ability to respond to stimulations, varying as we know in puberty and at the menopause.

An interesting observation is the facile interchange of nervous with hormonal impulses through the hypophysis. It is well known that the irritation of the cervix by a thread or by a glass tube in animals, as well as by a dissection or curettage in women, causes changes in the ovaries. That this is not due merely to an irritative hyperemia is shown by the fact that a follicle will rupture in an ovary transplanted far from the site of the irritative operation. It is also well known that psychic emotions, as well as changes in fat and vitamin metabolism, and imbalances in the vegetative nervous system, influence the ovary, and probably through the hypophysis.

In a previous paper I have demonstrated the correlation of lactation and pituitary function and the resulting alteration of the ovarian cycle.

From the above it appears rather probable that any changes, cyclical or otherwise, in the sex-generative organs may have far-reaching

TABLE I. TABULATION OF PITUITARY EXPERIMENTS*

PREPARATION OF THE DONOR ANIMAL	FINDINGS IN THE OVARIES OF THE DONOR ANIMAL	FINDINGS IN THE OVARIES OF THE IMMATURE MICE
Placental extract	FG : n L : +	FG : - L : +
Placental implant	FG : - L : ++	FG : + L : +
Folliculin	FG : n L : n	FG : n L : +
Corpus luteum extract	FG : 0 L : ++	FG : - L : ++
Urine of pregnancy	FG : - L : ++	FG : - L : ++
Suprarenin	FG : 0 L : ++	FG : n L : 0
Irradiation of the head	FG : 0 L : n Fibrosis	FG : n L : -
Irradiation of the head and placental implants	FG : 0 L : +	FG : n L : +
Irradiation of the ovaries	FG : 0 L : + Fibrosis	FG : - L : +
Oöphorectomy		FG : n L : +
Oöphorectomy and urine of pregnancy		FG : - L : +
Oöphorectomy and anterior pituitary extract		FG : - L : +
Pregnancy	FG : - L : +	FG : - L : +

*Luteinization: L. Follicular growth: FG. Normal: n. Increased: +. Extreme: ++. Diminished: -. No: 0.

influences, and especially on the anterior pituitary body. This fact may be of some value in the treatment of certain gynecologic conditions.

SUMMARY

1. Pituitary glands obtained from rabbits, guinea pigs, rats, and mice which had been treated with placental extract, placental tissue, corpus luteum hormone, folliculin, and urine of pregnant women, were implanted into immature mice. More lutein tissue and pseudocorpora could be seen in the ovaries of such mice as compared with those obtained from animals into which normal pituitaries had been implanted.

2. The promotion of follicular growth by the pituitaries of animals treated with folliculin or placental tissue was variable, but occasionally increased. This phenomenon was even less pronounced after injections of placental extract, corpus luteum hormone, and urine of pregnant women.

3. Injections of suprarenin do not increase the luteinizing action of the pituitary in transplants.

4. Implants of guinea pig, cat, and rat placenta into immature mice have only a slight effect on the ovary.

5. X-ray irradiation of the head does not increase the luteinizing power of the pituitary gland. On the other hand the pituitary of animals whose ovaries had been previously irradiated causes a distinct luteinization of the ovaries of the immature mice.

6. The continuous administration of corpus luteum hormone, placental extract or tissue, folliculin, and urine of pregnant women in adult rabbits, guinea pigs, rats, or mice, causes a luteinization of varying degree, attended with an alteration, or a suppression of the ovarian cycle.

7. The anterior pituitary does not store hormones.

8. The human placenta at term does not contain corpus luteum hormone.

10. The yellow body has a certain degree of independence of the ovum, as is shown by its continuing to function after removal of the latter.

CONCLUSIONS

By the use of extracts of the anterior pituitary body various investigators have shown that there are two different hormones in the anterior pituitary acting on the ovary: One stimulates the development of follicles, the other activates the lutein tissue. In this paper I have shown that the whole gland can produce both effects.

The anterior pituitary itself is influenced by endocrine substances of the ovary and the placenta. Consequently the anterior pituitary does not absolutely control the ovarian cycle. On the other hand a cyclic

function of the anterior pituitary, due to this reciprocity, is quite probable but not yet proved.

One must bear in mind that the injection or implantation of various substances may act either directly on the ovary of the immature mouse, or only indirectly, by having acted simultaneously on the pituitary gland of the test animal, and this introduces a possible error in our inferences.

I take great pleasure in thanking Dr. J. W. Williams for his interest in this work.

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MONILIA VULVOVAGINITIS*

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FUNGUS infections of the vagina have been recognized for nearly a century under various names,[†] but have latterly received but little attention. Only isolated reports of the condition have appeared in the recent literature and it is generally assumed that this type of infection is uncommon. With greater attention being paid to vaginal inflammations and their causative agents, it is evident that the rarity of this condition has been overemphasized, and that a study of the vaginal secretions in patients with vulvovaginitis will frequently reveal the presence of organisms of the *Monilia* group.

According to Castellani,¹ Wilkinson reported the presence of yeast-like organisms in the vaginal discharge in 1840 (*Lancet* 1: 1840), the year after Langenbeck had discovered the fungus in cases of oral thrush. Mayer² described the condition in 1862 and reported six cases, while others recorded isolated observations, but it was not until considerably later that these studies were extended by Haussmann³ and v. Winckel.⁴ A considerable literature then developed, but largely subsided about the end of the last century, with expressions of increasing doubt concerning the etiologic significance of the infection. More recently, isolated case reports have begun to appear again, and it seems wise to summarize the available information about the condition before recording our own observations.

Etiologic Relationship.—Among modern textbook authors, the majority, Kerr,⁵ Fulkerson,⁶ Crossen,⁷ Graves,⁸ and Frank⁹ assume the pathogenicity of the fungus but state that mycotic vaginitis is rare and usually mild. In the current literature, Le Blaye,¹⁰ Moench,¹¹ Davis,¹² Heard,¹³ Popoff, Ford, and Cadmus,¹⁴ Odland and Hoffstadt,¹⁵ Flusser,¹⁶ Perazzi,¹⁷ and Cordey,¹⁸ in reporting their experiences, assume the same relationship. On the other hand, Castellani and Taylor¹⁹ and Castellani²⁰ express some doubt, since the organism may be present in the vagina without producing symptoms. Finally, Stephan,²¹ supporting Zweifel's²² contention of the nonpathogenicity of the fungus, feels that the organism is not the chief etiologic factor in the inflammations with which it is associated, but that by excoriating the

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†Aphthous vaginitis; mycotic vaginitis; vaginal or cervical thrush; vaginal monilliasis; mycotic vulvovaginitis; colpitis mycotica acuta; vulvitis aphthosa; mycosis vaginalis; mycosis vaginae; saccharomycotic vulvovaginitis; vulvovaginite mycosique; muguet vulvovaginale; Soorkolpitis; Scheidenmykosen.

mucosa it permits the entrance of other microorganisms present in the profuse, mixed vaginal flora, and that these latter produce the inflammatory reaction.

Those, who have examined series of control cases, generally admit that *Monilia* may be present in the vaginal secretions of women who present no complaint of vaginal irritation. Haussmann³ found the fungi in 11 per cent of pregnant women who were without symptoms of vaginal irritation, and Moench¹¹ says: "Yeast cells are occasionally encountered in cultures from the normal cervix." Castellani and Taylor,¹⁹ on the other hand, state that, "In the normal vaginal secretion they (*Monilia*) are present, if present at all, in extremely scanty numbers, being found neither in smears nor in cultures."

Animal experimentation has not been conspicuously successful in demonstrating the pathogenicity of *Monilia* in the lower genital tract, although it must be admitted that few such efforts have been made. V. Winkel⁴ inoculated the vaginas of rabbits but produced only slight reddening of the mucosa, while Colpe,²³ using the same species, noted diffuse congestion, as well as a serous discharge, which appeared on the second day, increased for a few days, and finally disappeared after ten to twelve days. Two weeks after the inoculations, the fungi could no longer be demonstrated in the vaginas even by cultures. Haussmann³ inoculated a pregnant woman whose vagina was free from fungi with material taken directly from the vagina of another patient who had mycotic vaginitis. Nine or ten days later, vaginal burning and vulval itching appeared, to subside spontaneously within a few days, but to recur at intervals until active treatment was employed to destroy the organisms. In other instances, experimental inoculations of this sort, even with material from the mouth of an infant with oral thrush, produced only temporary heat and itching. It is interesting to note that inoculation of the vagina with brewer's yeast has been recommended as a therapeutic procedure in persistent leucorrhea, and reputedly with good results, Abraham.²⁴

Occurrence.—Yeast fungi are so widely distributed in nature, that it is perhaps surprising, that the organisms are not uniformly present in the vaginal secretions. It is generally recognized that pregnancy (any period of gestation after the first two months) and diabetes provide especially favorable conditions for the growth of *Monilia*, and that in the majority of cases no direct method of contamination can be detected.

Infection of a mother by *Monilia* from her thrush-infected child has been emphasized by Crossen,⁷ Giuliani,²⁵ and Mettenheimer.²⁶ Castellani¹ emphasizes the possibility of infection during intercourse, and Crossen⁷ stresses the diabetic husband, while Odland and Hoffstadt¹⁵ detail an instance where the husband contracted a *Monilia* balanitis following coitus with his wife who had mycotic vaginitis. Mettenheimer²⁷ and Flusser¹⁶ note patients, one a child of seven years, in whom vulval infections followed anginas due to the fungus.

The disease most commonly affects sexually active adults, with menstruation probably, and pregnancy certainly, a predisposing factor, although children are occasionally affected, Menge and Opitz.²⁸ Davis¹² states that many of his patients have already passed the menopause. The fact that parous women are more frequently attacked and that the disease may occur in women with uterine prolapse suggests that relaxed perineal structures favor accidental inoculation; but Mettenheimer²⁹ reports an infection in a virgin, and cases are not uncommon in nulliparous women,

whether pregnant or not. V. Herff³⁰ has pointed out that infections with irritative symptoms are much more common in warm, than in cold, weather, 20 of his 26 cases occurring in the summer half of the year. Castellani and Taylor¹⁹ intimate its greater frequency in the tropics, while Seely's³¹ statement of its occurrence in Texas lends confirmation to the idea that warm climates favor its appearance. V. Herff's³⁰ figures would indicate that the infection is more common among inhabitants of cities than in residents of rural districts. Direct association with commercial yeast, as in breweries and bakeries, has been cited as significant.

Incidence.—Haussmann³ found that 11 per cent of a series of women in the latter part of pregnancy harbored the organism without symptoms. V. Winckel⁴ noted 6 cases of mild mycotic vulvovaginitis, with only slight itching, among 150 pregnant women. During the course of almost seven years, v. Herff,³⁰ in the Halle Polyclinic, saw 24 cases of acute and subacute mycotic vaginitis among 13,283 admissions, an incidence of 1 in 553. Fifteen of these cases occurred among 2,010 pregnant women (1 in 134), while the remaining nine were seen among 11,273 gynecologic patients with various complaints (1 in 1,252). V. Herff excluded from his statistics those patients in whom the diagnosis could be made visually from the thrush-like patches on the vaginal mucosa. We have nowhere found figures for the nonsymptomatic occurrence of the fungus in nonpregnant women.

Type of Organism.—Using an old classification, v. Herff,³⁰ among 22 carefully studied cases, found the *Monilia albicans* 16 times, the *Monilia candida* 4 times, and the *Leptothrix vaginalis* and an unidentified yeast-like fungus once each. Castellani and Chalmers,³² following the former's complicated classification, based upon sugar fermentation reactions, have reported the occurrence of seven varieties of *Monilia* in patients with vaginitis (*M. balcanica*, *M. pinoyi*, *M. tropicalis*, *M. metalondinensis*, *M. naborri*, *M. parabalanica*, and *M. parapiinoyi*), as well as of fungi belonging to several other families. Popoff, Lord, and Cadmus¹⁴ identified the organism in their patient as *M. psilosis*, Ashfordi, a maltose-fermenter, similar to *M. pinoyi*, Castellani. Odland and Hoffstadt¹⁵ identified the *M. pinoyi* in one case.

Symptoms and Signs.—V. Winckel⁴ insisted that itching is the only common symptom, even though burning, especially after urination, smarting, pelvic fullness, and vaginal sensitiveness are frequently noted. Digital and speculum examinations, and coitus may be extremely painful. All symptoms tend to be aggravated at night. Remissions are common, and, in pregnant women, delivery usually brings relief from symptoms. Among nonpregnant individuals, the symptoms are usually worse in the premenstrual period, when the vaginal acidity is increased, in contrast to infections with the *Trichomonas vaginalis*, when discomfort is more pronounced during or just after menstruation, Davis.³³ Following an acute infection, the organisms may remain in the vagina for years without producing symptoms, or with occasional exacerbations followed by spontaneous relief.

The infection may, or may not, lead to the development of thrush-like patches on the vaginal, vulval, or cervical epithelium. When such localized growths are present, the lesion may resemble vaginal diphtheria, or may be similar to oral thrush. In other instances, and they are in the great majority, intense reddening of the mucosa of the labia minora, the introitus, and the vagina (particularly the lower third) occurs, with occasionally the development of a granular appearance suggestive of acute gonorrheal vaginitis. The irritation may involve the perineal skin and lead to the development of local intertrigo. Rarely furunculosis and superficial ulceration have been recorded.

Local edema may be present in severe cases, and condylomas, resulting from the chronic irritation, have been noted, Moench.¹¹ V. Herff³⁰ has maintained that there is an elevation of 0.5° to 0.8° C. in the vaginal temperature, without a general febrile reaction.

There is considerable difference of opinion about the character and amount of the associated vaginal discharge. Stephan²¹ claims that all his patients had previously had a noticeable leucorrhea, whereas v. Herff³⁰ obtained such a history in but 5 of 24 cases, and v. Winkel⁴ in only 1 out of six. During the acute infection, the discharge is generally said to be thin and highly acid, but not especially profuse, while in other cases it is thick and yellowish. In certain instances, white flakes appear in the discharge even though none can be seen on the mucosa.

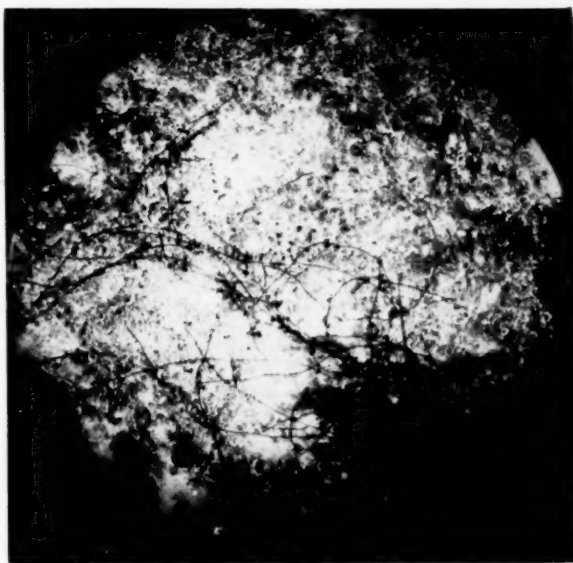


Fig. 1.—Monilia in vaginal smear. Mycelial and conidial forms. Photomicrograph, low power.

Complications appear to be rare, although Cordey¹⁸ records Monilia cystitis and bilateral lymphadenitis. There is slight evidence that the fungi may ascend into the cervical canal but not higher up in the genital tract.

Treatment.—Formerly, a great variety of local applications were recommended, but more recently gentian violet (Cooke,³⁴ Moench,¹¹ and Heard¹³), and alkaline douches and applications (Seely,³¹ and Popoff, Ford, and Cadmus¹⁴) have come to be generally employed. Faber and Clark³⁵ have found that gentian violet kills Monilia in a dilution of 1:25,000 and is more effective than other common antiseptics. Tanner and Bollas³⁶ report that, when incorporated into media, gentian violet

will destroy the fungi at a dilution of 1:80,000, and will definitely inhibit growth at 1:140,000.

Our attention was drawn to mycotic vulvovaginitis by the receipt in the State Laboratory of a smear from a six-months' pregnant patient with a severe vaginitis presumably of gonorrheal origin. After staining with Gram's stain, examination revealed no gonococci, but showed innumerable mycelial and bud forms of *Monilia*. Cultures on Sabouraud's media, obtained a few days later, developed a profuse growth of *Monilia*.

Shortly after this experience, a woman seven (lunar) months pregnant presented herself at the Out-patient Clinic complaining of the most severe and intense vaginal and vulval itching, which was making

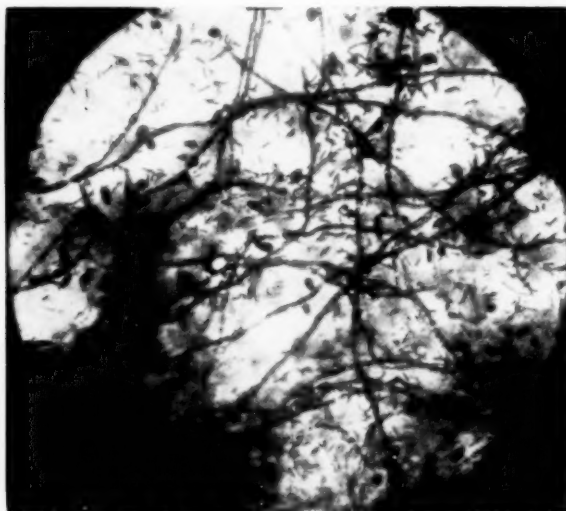


Fig. 2.—*Monilia* in vaginal smear. Photomicrograph, high-dry power.

her life miserable since she was constantly annoyed while awake and could not secure restful sleep at night. The vulva and vagina were the seat of a diffuse inflammation with reddening and irritation of the entire lower genital tract. The vaginal discharge was moderately profuse, clear, and extremely acid to litmus paper; no adherent exudate could be found on the vaginal walls, but there were a few white flakes in the secretion. Smears showed many mycelial and conidial forms of *Monilia* and culture gave a profuse growth of the organisms. Hanging-drop preparations revealed numerous *Trichomonads*. Treatment with 1 per cent aqueous gentian violet served to eliminate the *Monilia* infection and to relieve the symptoms almost entirely, even though the *Trichomonads* persisted. After delivery, neither *Monilia* nor *Trichomonas vaginalis* could be demonstrated, although the pa-

tient, a nervous individual, still complained of slight burning at times.

These experiences have led us to make an intensive study of vaginal infections with *Monilia* and *Trichomonas vaginalis*, although our interest in the latter organism has been secondary and dictated largely by a desire to learn whether it is constantly present in association with *Monilia*.

Smears and cultures were made from 63 patients complaining of more or less vaginal irritation, Table I; as well as from 85 patients free from such complaints and serving merely as controls, Table II.

Vaginal irritation was present in 18 pregnant women, among whom *Monilia* were demonstrated 12 times, an incidence of 66.7 per cent. Of the 5 primigravidas in this group, only 1 revealed *Monilia* (20 per cent), whereas 14 of the 16 multigravidas (87.5 per cent) showed the



Fig. 3.—*Monilia* in vaginal smear. Mycelial forms with budding elements. Note other organisms. Photomicrograph, oil-immersion.

organisms. Among 45 nonpregnant women presenting similar symptoms, only 11 (24.4 per cent) showed *Monilia*. Nulliparous women predominated in this group, 6 out of 11. These figures emphasize the fact that vaginitis in pregnant women is more frequently associated with *Monilia* infection than is vaginal irritation in the nonpregnant. The effect of previous childbearing is not evident among the nonpregnant group, although the relationship in the pregnant individuals is striking.

Monilia were demonstrated 15 times in the 46 pregnant patients in the control group, an incidence of 32.6 per cent, in the absence of irritative symptoms, although, in a few instances, it was possible to elicit a history of previous vaginitis. There were 30 primigravidas in the group with 11 cases of *Monilia* infection (36.7 per cent); while among

16 multigravidas, *Monilia* were demonstrated in 4 (25.0 per cent). Among 39 nonpregnant control patients, only 6 showed *Monilia* (15.4 per cent). A history of previous vaginitis was obtained in a few cases, although there was no way of determining whether this was related to a *Monilia* infection.

Patients in both the symptomatic and control groups were drawn largely from those admitted on the indigent service, although enough private patients were included to indicate that the condition is not limited by financial status or home surroundings. In fact, the most severe cases of vaginitis were observed in those well able to pay for their care and treatment.

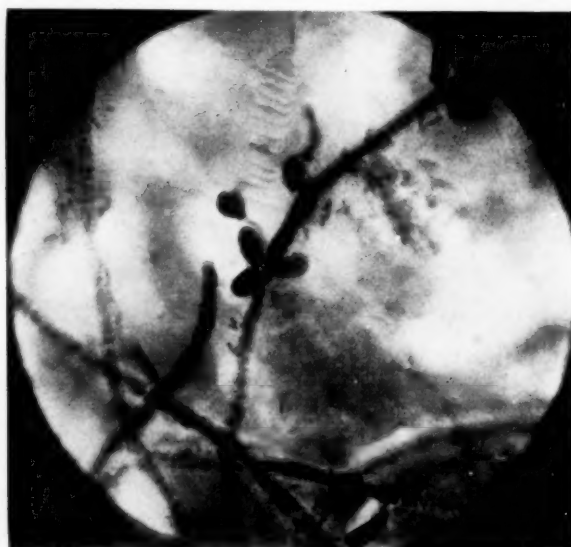


Fig. 4.—*Monilia* in vaginal smear. Mycelial forms with a few buds. Note granular character of protoplasm. Photomicrograph, oil-immersion.

The usual complaints were of burning, smarting on urination, and vulval itching, varying from slight discomfort to an irritation more severe than we have seen in any other form of vaginitis. Variations in the severity of the symptoms from day to day and week to week were frequently noted, with a considerable tendency toward spontaneous symptomatic cure. In the nonpregnant, relief was commonly experienced during the postmenstrual period, with exacerbations shortly before menstruation. (In *Trichomonas vaginalis* infections the situation is usually reversed, with the maximum discomfort after the cessation of the menstrual flow.) In pregnant individuals, delivery usually resulted in complete relief, although occasionally the symptoms persisted and became chronic, defying the more common efforts at control, until the apparent etiologic factor had been determined. In one instance, the patient (a physician's wife) suffered considerably with

vaginal irritation from the third month of her first pregnancy but was relieved by delivery. In the second gestation, burning and itching appeared again at the third month and persisted until parturition. The third pregnancy was similar except that the symptoms reappeared during the late puerperal period and recurred at frequent intervals for three years following the birth of this child. Attempts to establish a diagnosis based upon etiology and to effect a cure were of no avail until we discovered that the vaginal secretion was loaded with mycelial and conidial forms of *Monilia* (*M. pinoyi*, Castellani), when two applications of 1 per cent aqueous gentian violet produced complete cessation of symptoms.

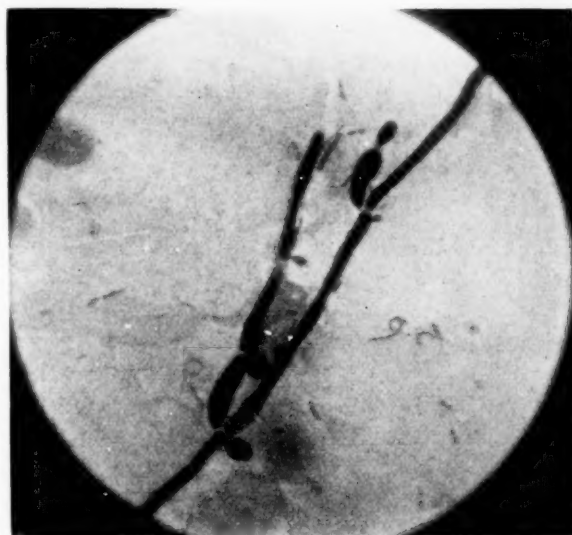


Fig. 5.—*Monilia* in vaginal smear. Mycelium showing segmentation, with budding and branching at segment junctions. Photomicrograph, oil-immersion.

Spontaneous relief or even symptomatic cure by nonspecific agents is frequently noted, and the organisms may then remain in the vagina for some time without giving rise to irritation. Probably certain of the individuals who show fungi without irritative symptoms fall into this group, although in many of them no such sequence of events can be elicited. Shortly before our attention was attracted to *Monilia* vaginitis, a young unmarried woman was admitted to the hospital because of intense vaginal irritation of several days' duration. Speculum examination, which was extremely painful, showed the entire cervix covered with a heavy, greyish-white membrane, which, when removed, left small bleeding areas, suggesting the membrane of diphtheria. Smears and cultures were negative for the Klebs-Loeffler bacillus, and no pathogenic organisms, with which we were familiar, could be found. Under symptomatic treatment, and after electric cauteriza-

tion of the cervix, the symptoms were completely relieved and no recurrences were noted. Some time after this episode, the patient married and recently returned for antepartum care when three months pregnant. There were no symptoms of vaginal irritation and the vagina appeared normal except that the mucosa was more reddened than is usual at that stage of gestation. Smears and cultures showed a plentiful growth of *Monilia*, and on the basis of this finding we are inclined to believe that the earlier severe symptoms were due to a *Monilia* vaginitis.

It is well known that *in vitro* the *Monilia* grow better in media with a considerable degree of acidity, Sabouraud's media is adjusted to a P_H of 5.5. Very probably, increased acidity of the vaginal secretion tends to make possible their growth where they have previously been absent,

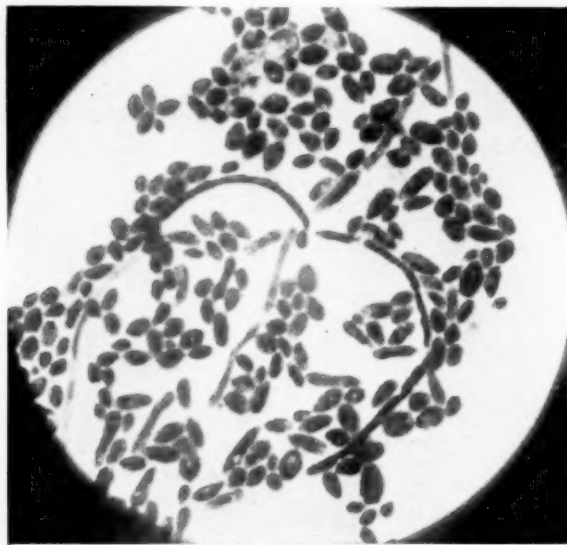


Fig. 6.—*Monilia* in culture. Many bud forms but few mycelial threads. Photomicrograph, oil-immersion.

or to augment their growth where they are constantly present. This would explain partially the fact that pregnancy promotes development of the fungi, so that their frequency either with or without irritation is markedly increased over the nonpregnant state. It is, of course, also possible that the availability of suitable food material is likewise a factor in determining the rate of growth and may explain directly the predisposition of diabetics to the infection. We have examined the secretions in five patients with undoubted diabetes, and in each instance have been able to demonstrate the *Monilia*, although in only one patient was there a complaint of irritation. That the actual presence of dextrose in the urine is a determining factor in the growth of the organisms and in the development of symptoms in diabetic individuals is suggested by the experience of Perazzi,¹⁷ who treated a diabetic with insulin and diet

management and noted relief of the vaginitis without the aid of local applications. It would seem very probable that, in patients with so-called diabetic pruritus vulvae, the irritation may be due to the presence and growth of *Monilia* with the resulting increased vaginal acidity, rather than to chemical action of the glucose itself, as has been usually thought. We have not had the opportunity to examine a patient with a well-marked diabetic pruritus, but the observations noted above support such a view. It has also occurred to us that the prevalence of the infection in pregnant women may be related to the known decreased sugar tolerance during that period, but none of our patients with positive cultures showed more than a very transient excretion of copper-reducing substances in the urine.

In several patients with postoperative pyelitis, conidia have been detected in the catheterized urine and *Monilia* isolated by culture, but we hesitate to attach any significance to the finding.

The vaginal secretion is in no way characteristic unless it happens to contain white, thrush-like flakes, which are highly suggestive. Leucorrhea is not a common complaint, although upon direct questioning it may be learned that there has been some increase in secretion, which tends to be thin and watery. The reaction of the secretion is generally very acid, but occasionally the organisms are found with a nearly neutral discharge.

The vaginal mucosa is reddened in the presence of irritative symptoms and may be granular in appearance in severe cases, resembling the condition so frequently seen in marked cases of gonorrheal vaginitis. Occasionally, small ulcerated areas can be located upon the mucosa or upon the surrounding skin, where a real intertrigo may develop. Thrush-like patches of exudate upon the vaginal or cervical mucosa are noted only occasionally in spite of the common statement that they constitute an important diagnostic sign. When such an exudate is found, it is almost pathognomonic of *Monilia* infection, but its absence does not by any means exclude this type of involvement.

Inguinal lymphadenitis was not observed in any of our cases, and apparently is only rarely found.

Painful coitus is an occasional complaint, while digital and speculum examinations may produce extreme pain and marked levator spasm, especially in nulliparous women.

Diagnosis may be made from hanging-drop preparations by finding mycelial threads with their budding elements, but where mycelia are absent, it is only by stained smears and by cultures that a positive diagnosis can be made. Both the mycelial and conidial forms stain well with the usual dyes, and are markedly gram-positive.

Sabouraud's media (dextrose-peptone-agar, adjusted to a P_H of 5.5) is best adapted to detection of the fungi in doubtful cases or for confirmation, since the high degree of acidity interferes with the growth

of most of the other organisms commonly present, although certain strains of staphylococci and a few bacillary forms grow abundantly. The *Monilia* develop rapidly as white, greyish-white, or cream-colored, elevated, glistening colonies of considerable size. Pure cultures are easily obtained by spread planting on Sabouraud's plates. In recent cultures, the conidia predominate, and it may be impossible to find mycelial forms; but in older cultures in liquid media and in the fluid at the bases of old slant cultures mycelial forms may be numerous. On old carrot cultures, the mycelia sometimes grow so profusely as to form a tenaceous membrane.

Classification of the *Monilia* on the basis of their fermentation reactions in various carbohydrate media is very confused because of the multitude of minor variations, as well as from the fact that different investigators have applied different names to what is apparently the same fungus. Moreover, Castellani and Taylor¹⁹ insist that "many *Monilia* after a few transplantations lose some of their fermentative characters or these are altered. Hence the determination of species is possible only using recently isolated strains." The few strains which we have isolated have remained remarkably constant after months of cultivation. We have followed Castellani's classification as far as possible, since it is more widely employed in this country, in spite of the difficulties which it entails. The strain most commonly met ferments dextrose, levulose, and maltose with the formation of acid and gas, but does not attack the other sugars (*M. pinoyi*, Castellani), although other forms are occasionally isolated. Table III indicates that in 39 cases where the vaginal organisms have been studied culturally, *M. pinoyi* was found in 28, *M. krusei* in 6, and *M. metalondinensis* in 1, while 4 fungi gave atypical reactions and remain unclassified. It is interesting that the organisms more commonly isolated, *M. pinoyi* and *M. krusei*, produced irritation in approximately the same percentage of pregnant and nonpregnant women. Castellani and Taylor¹⁹ report having isolated seven strains of *Monilia* from the vaginal secretions, but do not mention *M. krusei*, which we found in 6 individuals, 4 with and 2 without vaginitis.

Tables I and II present data on the appearance of the *Trichomonas vaginalis* in certain individuals studied especially for *Monilia*. The percentage incidence of these organisms is practically the same in the various groups, and corresponds well with the average recorded incidence (40 per cent) as noted by Greenhill,²⁷ except that pregnant patients in the control group have an unusually low incidence (15 per cent). *Trichomonas* and *Monilia* may exist together or separately in the presence or absence of irritation. In a few instances, the *Trichomonads* were detected in the absence of *Monilia* in patients who had mild vaginitis, but we are still undecided whether they were actually causing the irritation or were merely innocent secondary invaders.

In at least one case of combined infection, the irritation was relieved by treatment leading to disappearance of the *Monilia*, although the *Trichomonads* were still present in considerable numbers. It is quite evident that either organism may exist in the vagina entirely independent of the other, as well as in symbiosis.

TABLE I. SIXTY-THREE PATIENTS WITH VAGINAL OR VULVAL IRRITATION

	MONILIA PRESENT	MONILIA ABSENT
Pregnant	12	6
With <i>Trichomonas</i> infection	4	3
Without <i>Trichomonas</i> infection	4	1
Not examined for <i>Trichomonas</i>	4	2
Nonpregnant	11	34
With <i>Trichomonas</i> infection	2	10
Without <i>Trichomonas</i> infection	3	12
Not examined for <i>Trichomonas</i>	6	12

TABLE II. EIGHTY-FIVE CONTROL PATIENTS WITH NO VAGINAL OR VULVAL IRRITATION

	MONILIA PRESENT	MONILIA ABSENT
Pregnant	15	31
With <i>Trichomonas</i> infection	1	1
Without <i>Trichomonas</i> infection	5	6
Not examined for <i>Trichomonas</i>	9	24
Nonpregnant	6	33
With <i>Trichomonas</i> infection	2	5
Without <i>Trichomonas</i> infection	2	10
Not examined for <i>Trichomonas</i>	2	18

Twenty-four pregnant women with *Monilia* in the vaginal secretions have been delivered, and four of the babies developed oral thrush shortly after birth without seemingly having been exposed to an ordinary nursery infection. In one instance, the child was born at home and in another the oral infection developed when the child was in a newly-opened nursery, where thrush had never appeared. The other two cases occurred when there were no known cases of thrush in the nursery. The possibility of oral thrush developing from *Monilia* transferred directly or indirectly from the contaminated vaginal secretions of the mother has been confirmed experimentally. The details of this investigative work will be reported separately, but it can be stated here that pure cultures of *Monilia pinoyi* obtained from the secretions of both pregnant and nonpregnant women, with and without vaginal irritation, as well as those found in the sputum of a male patient with pulmonary moniliasis have invariably produced oral thrush when inoculated into the mouths of healthy newborn children, whereas other strains of the fungus have never led to clinical thrush although the organisms were recoverable from the mouths for several days after the inoculations.

Gentian violet, in 1 per cent aqueous solution, appears to be an almost specific therapeutic agent. The vagina is exposed with a bivalve speculum and the entire mucosa swabbed generously at daily or bi-daily intervals. Frequently two or three applications are sufficient to relieve the itching, although longer treatment is probably necessary to eradicate the organisms completely. Alkaline douches of sodium bicarbonate or borax are useful at times to relieve irritation and may actually prove curative by reason of the action of the alkali.

TABLE III. TYPES OF MONILIA ISOLATED FROM VAGINAL SECRETIONS

TYPE OF MONILIA	PREGNANT		NONPREGNANT	
	WITH IRRITATION	WITHOUT IRRITATION	WITH IRRITATION	WITHOUT IRRITATION
<i>M. pinoyi</i>	10	8	6	4
<i>M. krusei</i>	2	2	2	0
Unclassified	1	2	1	0
<i>M. metalondinensis</i> in 1 culture from the outside, poor history, no irritation.				

TABLE IV. CULTURAL REACTIONS OF OBSERVED MONILIA

TYPE	DEX-TROSE	LEVULOSE	MALTOSE	GALACTOSE	SACCHAROSE	DEXTRIN	INULIN
<i>M. pinoyi</i>	⊗	⊗	⊗	—	—	—	—
<i>M. krusei</i>	⊗	⊗	—	—	—	—	—
<i>M. metalondinensis</i>	⊗	⊗	⊗	⊗	—	—	—
Unclassified No. 1	⊗	⊗	+	—	⊗	—	—
Unclassified No. 2	⊗	⊗	+	+	—	+	+
Unclassified No. 3	⊗	⊗	+	+	⊗	—	—
Unclassified No. 4	⊗	⊗	+	⊗	⊗	—	—
0 = gas		+ = acid		⊗ = acid and gas			

DISCUSSION

Monilia are abundant in the vaginal secretions of certain patients who suffer from more or less severe vulvovaginitis, but the fact that apparently identical organisms may be recovered from other individuals with no history of vaginal irritation naturally raises some doubt as to the pathogenicity of the fungus. Haussmann's³ single, successful human experiment suggests a positive etiologic relationship, and our clinical experience supports this contention, but we feel that more extensive work should be done before a definite scientific pronouncement can be made. The situation is comparable to that which exists in regard to the *Trichomonas vaginalis*, where diametrically opposite opinions concerning its pathologic significance are still firmly held. Our studies would indicate that this latter parasite may, on occasion, be the cause of a definite, specific vaginitis, although again concrete experimental proof of a cause-and-effect relationship is lacking. When the two organisms, *Trichomonas* and *Monilia*, are present simultaneously, our experience would suggest that the latter is more probably responsible for the symptoms, so that treatment to eradicate the fungus is indicated.

The presence of *Monilia* in the vaginal secretions of pregnant women offers a definite avenue for development of oral thrush in the newborn through contamination of the mouth directly or indirectly. On this point, we feel secure, since we have shown experimentally that pure cultures of *Monilia*, isolated from vaginal secretions, will result in clinical thrush when placed in the mouths of newborn infants, and that it is possible to recover the organisms from the lesions thus produced. Thus far experimental thrush has been developed only after inoculation with one species of *Monilia*, *M. pinoyi*, Castellani.

CONCLUSIONS

1. *Monilia* are frequently present in the vaginal secretions of patients suffering from vulvovaginitis, and appear to be concerned directly with the etiology of the clinical condition, although normal individuals may harbor the fungi for long periods without showing vaginal irritation.

2. Pregnancy and diabetes are definite predisposing factors, and menstruation may be, since sexually active women are more prone to the infection. Parous women are more often infected, but children, virginal adults, and senile women may likewise show the organisms. In the majority of instances the mode of infection cannot be demonstrated. High acidity of the vaginal secretion favors the growth of *Monilia*, but is not essential.

3. The chief symptoms of the infection are itching, burning, and smarting of the lower vagina and vulva. Digital and speculum examinations, and coitus are painful. A profuse leucorrhea rarely appears, and only occasionally is the secretion characteristic, when it contains small white flakes of thrush-like material. Varying degrees of vaginitis are encountered, with, occasionally, the appearance of definite vaginal or cervical thrush. Complications are rare.

4. *Monilia* vaginitis tends to undergo spontaneous relief, but occasionally becomes chronic and may produce recurrent irritation over a period of months or years. Delivery usually leads to complete relief in pregnant women, while menstruation generally has the same effect temporarily in the nonpregnant.

5. Gentian violet, in 1 per cent aqueous solution, applied locally affords the best method of treatment. Alkaline douches may be of some value.

6. *Monilia* vaginitis in pregnant women is a definite source of infection in sporadic outbreaks of oral thrush in the newborn.

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The author maintains that all women with gonorrhea and with uterine bleeding not due to malignancy can be cured by nonoperative measures. Many cases of sterility may likewise be treated conservatively. The use of intrauterine instillations is advocated because it stimulates tissues through the blood. The author employs silver preparations because they produce a marked local hyperemia and iodine solutions because they are useful as iodine-ion therapy. The author claims to have obtained excellent results in cases of salpingitis and uterine bleeding by this form of treatment.

J. P. GREENHILL.

A CASE OF FLOATING UTERUS WITH CALCIFIED PEDUNCULATED FIBROIDS PRESENTING ANEURYSMS OF THE AORTA AND RIGHT INNOMINATE ARTERY

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ACCORDING to Graves, pedunculated fibroids are not uncommon. The same author describes floating fibroids. These are subserous myomas that become detached from their pedicles and float out into the abdominal cavity. However no mention is made of the occurrence of a floating uterus. None of the standard textbooks describe such a condition. A search of the available literature fails to reveal a case in which the entire uterus floats freely in the abdominal cavity suspended aloft by an elongated cervix acting as a pedicle. Because of the rarity of the condition and the diagnostic difficulties it presented, the following protocol is reported.

S. R., aged sixty, a colored female, was admitted to the medical service of Lincoln Hospital on December 25, 1929. The patient, apparently, had been perfectly well until the morning of admission, at which time she became suddenly unconscious and fell to the floor. There was no history of previous similar attacks. On arrival at the hospital the patient regained consciousness but was unable to move her right arm and right leg. There was no story of vomiting; no urinary difficulties; and no abdominal pain. It was learned that she had had no bowel movement for three days. There was little of special significance in her previous medical history. She had had one pregnancy to term with death of the child in early infancy. There had been no miscarriages and venereal infection was denied. The family history was irrelevant.

Physical Examination.—The patient was an emaciated colored female, somewhat stuporous. The right side of her face was flattened. A marked *arcus senilis* was present. The right pupil was larger than the left, and was irregular and fixed. The left pupil reacted to light. The tongue deviated slightly to the right. There was an irregular expansile mass on the right side of the neck over which a systolic bruit could be heard. The lungs were clear except for a slightly prolonged expiratory note. The area of precordial dullness was enlarged both to the right and to the left. At the level of the sternal notch it measured $4\frac{1}{2}$ cm. to the right and 7 cm. to the left of the midsternal line; at the level of the xiphoid it was $6\frac{1}{2}$ cm. to the right and $9\frac{1}{2}$ cm. to the left of the same line. A loud systolic murmur of musical quality was heard over the entire precordium. No thrills were felt. The radials were thickened and easily palpable. The blood pressure was 220/110. Abdominal examination revealed a large, stony-hard, nodular and non-tender mass in the right lower quadrant. It was freely movable and could be shifted to either side. Subsequently this mass was felt under the right costal margin, in the right inguinal region and in the left lower quadrant. On pelvic examination the vagina was found to be very long; the cervix was made out with difficulty, and the uterus was not felt. The large abdominal mass was not palpable on bimanual manipulation. Neurologic examination showed no definite evidence of a hemiplegia.

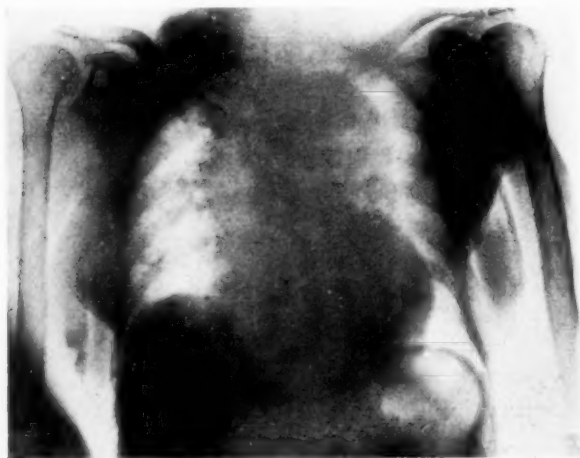


Fig. 1.—X-ray of the chest showing an aneurysmal dilatation of the aorta with calcified areas in the ascending aorta and aortic arch.



Fig. 2.—A flat plate of the abdomen taken after a barium enema, showing an opacity, not unlike an accumulation of barium in the cecum and ascending colon. This opacity was due to the calcified fibroid uterus.

Laboratory Observations.—The blood Wassermann was 4-plus with both the alcoholic and cholesterol antigens. The blood urea was 18.44 mg. per 100 c.c. The blood sugar was 0.173 per cent. A catheterized specimen of the urine showed a specific gravity of 1030, the reaction was acid and it contained a very faint trace of albumin and also a faint trace of sugar. The microscopic examination was negative. An x-ray of the chest showed an aneurysmal dilatation of the entire aorta with calcified areas in the ascending aorta and aortic arch. (Fig. 1.)



Fig. 3.—Pyelogram of the right kidney showing that the mass has no relationship to the right renal pelvis or calices.

Treatment and Course.—It was thought at the time that the abdominal mass represented a fecal impaction. The patient was put on oil enemas followed by colonic irrigations and was also given mineral oil by mouth. After a thorough trial of this régime had failed to influence the size of the mass, a flat x-ray plate of the abdomen was taken. This revealed an opacity in the right side of the abdomen not unlike an accumulation of barium in the cecum and ascending colon, this, despite the fact that the patient had not received a test meal. A barium enema was then given but was not retained completely. (Fig. 2.) On January 10, following the administration of magnesium sulphate the patient had a spontaneous bowel movement. Catharsis produced no change in the size of the mass.

On the assumption that the tumor might be a gummatous infiltration, large doses of potassium iodide were given. This therapy was ineffectual. At this time, after further x-ray study, Dr. Gottlieb reported that the mass had no relationship to the cecum or ascending colon. It was then suggested that we might be dealing with a calcified kidney. Cystoscopy was done and a pyelogram of the right kidney was taken. This showed that the mass had no relationship to the right renal pelvis or calices. (Fig. 3.) Following cystoscopy the patient developed a low grade fever, gradually became weaker and died on February 25, 1930.

Postmortem Findings.—The body was emaciated and weighed about 90 pounds. There was no edema or jaundice. The pleural cavities and the pericardial sac showed no excess of fluid or adhesions. The heart showed hypertrophy of the walls more marked on the right side. The cavities were moderately dilated. At the base of the aortic valve there was an ulceration of the endocardium measuring about 1 cm. across. From the aortic leaflets to the proximal portion of the descend-



Fig. 4.



Fig. 5.

Fig. 4.—Anterior view of the uterine mass showing the pedunculated fibroids.

Fig. 5.—The body of the uterus has been incised longitudinally and a probe has been inserted through the external os. It is seen emerging from the internal os into the uterine cavity.

ing abdominal aorta, there was found a marked dilatation of the wall with severe scarring, puckering, and plaque formation of the inner surface. An aneurysmal bulge was observed in the descending portion of the aortic arch. The right innominate artery showed marked dilatation with thinning and bulging of the wall. The lungs, liver, spleen, pancreas, stomach and intestines showed no pathology. The left kidney presented some scar-formation and its capsule stripped with difficulty. The right kidney contained multiple cortical abscesses, several of which had perforated through the capsule and were surrounded by adhesions. No abscesses were found in the medulla. The pelvis of the right kidney was injected but the ureter was patent.

The uterus lay free in the abdominal cavity, suspended by an elongated cervix (12½ cm. in length) which had the appearance of a thinned-out sheet of mesentery.

The vaginal canal was likewise elongated and measured approximately 11 cm. in length. The body of the uterus was considerably deformed by intra- and extra-mural calcified myomas. (Fig. 4.) Two pedunculated fibroids extended upward from the uterus. Both of these were completely calcified and could not be sectioned with a sharp knife. The cervical canal was patent and a probe could be passed upward into the cavity of the uterus without any difficulty. (Fig. 5.) The adnexa showed no pathology.

Anatomic Diagnosis.—(1) Syphilis; (2) syphilis of the aorta with aneurismal dilatation; (3) generalized arteriosclerosis; (4) aneurism of the right innominate artery; (5) calcified fibroid uterus; (6) cortical abscesses of the right kidney; (7) ulceration of the endocardium at the base of the aortic leaflet.

COMMENT

This case presented many interesting features. Although the history as related by the patient was not completely reliable it is quite definite that the abdominal mass gave no symptoms. Marked obstipation of several days' duration led to a firm belief that the mass was produced by a fecal impaction. Cabot has already pointed out that the diagnosis of fecal impaction is usually an erroneous explanation of any abdominal tumor. It proved to be so in this case. The probability of a gumma of an abdominal viscus was seriously considered, because of the clinical and serologic evidence of syphilitic infection. Failure to change the size of the mass by the administration of large doses of potassium iodide militated against this diagnosis. Early x-rays, showing an opaque mass, suggested a tumor of the cecum or even a calcified kidney but these possibilities were excluded by further study. To complicate our problem, pelvic examination tended rather strongly to negate the probability of any gynecologic pathology.

CONCLUSION

A study of the foregoing case shows that a mobile tumor of the abdomen may be a floating uterus. Furthermore, if a uterus is not palpable on bimanual examination there is a possibility that its position may be altered by an elongated cervix.

1964 GRAND CONCOURSE.

190 ALEXANDER AVENUE.

THE MIOSTAGMIN REACTION IN THE DIAGNOSIS OF UTERINE CANCER

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IN A RECENT paper, Green¹ reported very favorable results on the application of the miostagmin reaction in the diagnosis of tumor. He obtained a positive reaction with carcinoma and a negative one with human sarcoma. Such results suggested the use of this reaction, particularly for the determination of the presence or absence of carcinoma in the radium-treated uterine cancer cases in Dr. George Gray Ward's follow-up clinic.

The miostagmin (*meion*: less; *stagma*: drop) reaction depends upon the reduction of surface tension of certain sera in the presence of an "antigen," thereby giving an increased number of drops as measured by a special pipette, the Traube stalagmometer.

In 1910, Ascoli² first applied this reaction to the diagnosis of typhoid fever. He believed the reaction to be specific, since the diluted antigen (alcoholic extract of typhoid bacilli), mixed with a diluted typhoid immune serum, gave a definite reduction in surface tension as compared with a normal serum. Since that time, numerous investigators, employing various so-called antigens, have extended the application of the reaction to the diagnosis of malignant tumors. Grevé,³ in 1924, used the saturated fatty acid, normal caproic acid, as the antigen because of its stability, and obtained a positive reaction in all of his carcinoma cases.

The miostagmin reaction is obviously not specific, since a positive reaction may be obtained in certain conditions other than carcinoma, such as in pregnancy, nephritis, cirrhosis of the liver, arthritis, uremia, advanced pulmonary tuberculosis, and in many feverish conditions. Nevertheless, these conditions can be readily recognized and do not detract from the value of this reaction in those cases in which the miostagmin reaction may be an aid to the clinical observations in making a proper diagnosis. In this paper, it will be shown that the miostagmin reaction may be useful in determining the prognosis of many cases of radium-treated uterine cancer.

Green states: "The large number of authors who have employed the miostagmin reaction for the diagnosis of cancer unanimously agree that the reaction is of indisputable value and has already been observed by Roosen and Blumenthal and later by Burmeister, 'a decidedly negative reaction is of more value than a positive one and may be considered of some weight in ruling out carcinoma.' 'Of all cases of carcinoma examined, not one gave a negative reaction.' (Grevé.) The assertion of this author is also confirmed by Wissing thus: 'There is not the least

doubt that the reaction will give valuable diagnostic information where the usual method of investigation fails.' Kelling emphasizes the importance of the reaction as a great practical aid, especially in differentiating between malignant and benign growths of the digestive tract.

"One of the most important requisites of the miostagmin reaction seems to be its very early appearance as compared with the other means of investigation at our disposal. 'The sensitivity of the reaction is a relatively great one in that the reaction in an early stage may already be positive' (Waterman). This has also been confirmed by Wissing, who says: 'In each of 9 patients with carcinoma varying from the size of a cherry to that of a walnut, all gave a marked meostagmin reaction.' Wissing also notes that 'The most important fact is that the miostagmin reaction is also negative in all those clinical conditions which could be easily mistaken for cancer, such as benign tumors, gastric ulcer, chronic enteritis and colitis, ulcus cruris, in surgical tuberculosis without fever, in chronic inflammation of the female genital organs, and in syphilis.' One might also add 'in sarcoma.'"

Green's own work with the Grevé antigen and the Traube stalagmometer gave the following results:

"Out of 25 cancerous sera, 23 gave a positive and 2 a negative reaction; of 25 sera in which carcinoma was clinically excluded, 8 gave a positive and 17 a negative reaction; 7 sarcomatous sera all gave a negative reaction; and 16 normal sera all reacted negatively."

METHOD

In this study Grevé's antigen and technic were employed.

The antigen, normal caproic acid (Eastman Kodak Co.), was diluted with 0.85 per cent NaCl solution in the ratio of 0.1 c.c. antigen to 220 c.c. saline solution. This diluted solution of antigen will be designated hereafter as "antigen solution." The test is made by adding 9 c.c. of 0.85 per cent NaCl solution to 1 c.c. of serum in a test tube. This acts as the control. In a second test tube, 9 c.c. of antigen solution is added to 1 c.c. of serum. Both tubes are heated at the same time for one hour at 50° C. and cooled spontaneously for two hours at room temperature. The count is then made with the Traube stalagmometer for both the control serum and the antigen treated serum. *Normal sera should give a difference of less than two drops; whereas carcinoma sera, more than two drops.*

The above information is insufficient for obtaining proper and reproducible results. It is essential for the attainment of precision that will permit satisfactory reproducibility of results that all conditions should obviously be comparable. Therefore, to attain good precision, it is necessary that the following precautions should be observed:

1. *Clean Glassware.*—All glassware should be properly cleansed with chromic acid solution, washed thoroughly, and rinsed with distilled water. The stalagmometer should be cleansed between each run of control serum and antigen treated serum—first with water (sucked through), then chromic acid, followed by several washings with distilled water. Drying may be hastened by cautiously heating the bulb and stem of the stalagmometer with a Bunsen burner to the point barely tolerable to the fingers. The surface of the stalagmometer at which point the drop of diluted serum forms, should under no circumstances be touched by the fingers. Greasing of this surface vitiates the results, since the surface will not be wet alike by the control serum and the antigen-treated serum. No alcohol or ether should be employed for drying the apparatus, inasmuch as a slight amount of these chemicals will, of their own accord, reduce surface tension of the diluted serum.

2. *Preparation of Solutions.*—The saline solution is prepared from some high-grade analytical or recrystallized C.P. sodium chloride.* The distilled water should be boiled before use, cooled quickly, and used immediately, or else should be stored in a container well stoppered. Sufficient saline solution is made up so that a portion can be used for the preparation of the antigen solution. It is very important that *exactly* 0.1 c.c. of the n-caproic acid should be measured out and diluted with 220 c.c. of 0.85 per cent saline solution. As a further additional precaution to check the purity of the n-caproic acid, the proportions as given above should strictly be adhered to; in addition, runs should also be made on a normal serum or sera with slight alteration of the antigen content. This can readily be accomplished, for example, by the addition of 1 c.c. of saline solution to the 1 c.c. of serum before the addition of the 8 c.c. of antigen solution to make the necessary 1:10 dilution. If the values for the drop difference for normal sera are about 1.5 drops, one can then be assured of having proper reagents for doing the miostagnin reaction.

3. *Stalagmometer Readings.*—The whole number of drops can readily be counted, but since a fraction of a drop throws a result either to the positive or negative direction, it is very essential that the *starting-point* should be identical in all cases and that the *end-point* should be read just when the drop has left the stalagmometer with the meniscus of the diluted serum still somewhere in the lower calibrated capillary portion of the stalagmometer.

(a) The starting-point may be attained first by lightly touching a clean, dry filter paper to the drop-formation surface and carefully wiping with filter paper the ground edge; then the diluted serum should be permitted to descend just to the top mark in the upper calibrated capillary portion of the stalagmometer; finally a clean, dry glass rod ($\frac{1}{4}$ " in diameter) is carefully brought up to the partial drop with the long dimension of the rod parallel to the drop-formation surface of the stalagmometer. The drop is squeezed to within a millimeter of the drop surface of the stalagmometer and the excess of the drop is removed by the withdrawal of the glass rod. This method insures good reproducibility, as demonstrated by a number of runs made on the saline solution.

(b) The end-point is read while the diluted serum is still in motion. With a little practice, one can determine the meniscus reading in the lower calibrated capillary, just when the drop leaves the surface. Previous calibration with our own stalagmometer showed that 21 divisions were equivalent to one drop. If the drop came off above the entirely circumscribed end-point, then the required number of divisions were added to bring the result to the fixed definite volume. On the other hand, if the drop came away at a point where the reading on the capillary was below the circumscribed end-point, then just so many divisions were subtracted from a whole drop. By this method one could determine the end-point very precisely—the error might at times be 5 per cent of a drop.

4. *Temperature.*—One assumes that if the surface tension of both the control and the antigen sera were determined at the same room temperature, then the requirements of precision would properly be satisfied. Such is not the case. Experimental data, derived with my serum, indicate that the higher room temperature as encountered in our laboratory may cause a marked error. The necessary temperature correction is shown in Table I.

The numerals under columns "Saline" and "Antigen" indicate the requisite number of divisions to be subtracted from respective readings in order to correct to 25° C. (N. B. 21 divisions equal 1 drop.)

*In this work, Merck's C. P. sodium chloride was employed.

Of course, if the apparatus and sera could be immersed in a thermostat, then all the data would be obtained under identical temperature conditions and the necessity for temperature corrections would thereby be avoided. A number of temperature curves should be made for various normal and pathologic sera to obtain the approximately true curve for temperature correction. In our present work, we took the temperature of the diluted serum immediately after it left the stalagmometer, by the immersion of a thermometer in the fluid.

TABLE I

TEMPERATURE	SALINE	ANTIGEN
25.5° C.	2	3
26.0	3	6
26.5	5	9
27.0	7	12
27.5	8	16
28.0	11	19
28.5	13	23
29.0	16	27

5. *Blood Serum*.—When a dry sterile needle and syringe are employed, one need not be concerned with any special precautions for the withdrawal of blood from the patient's vein. But, as in our present series, to permit a large number of cases to be tested in the limited time at our disposal, the routine procedure of taking blood specimens should be modified in this respect, that dry sterile needles should be employed and the syringe should be carefully rinsed in two changes of sterile 0.9 per cent saline solution. If this procedure were not adhered to, then invariably some of the sera would show hemolysis owing to the alcohol retained in the needle when alcohol was employed for sterilizing it. The tourniquet should not be too tight or left on too long, since stasis does alter to a slight extent the protein concentration of the serum.⁴ Hemolysis also increases the serum concentration. The samples of blood should preferably be drawn before breakfast, so as to avoid lipemia so frequently found in the ambulatory clinic patients. A light breakfast avoiding butter, cream, and fried stuff, will not interfere with the test as shown by our results in all of the tables. We were unable to draw any specimens of blood before breakfast in our cases. It is essential that the ambulatory patient or individual be at rest for at least twenty minutes before drawing the blood. Rowe¹ has shown a great increase in protein concentration in the serum even when an individual does no active work except walking about for a few minutes. The clinic patients were at rest for more than twenty minutes when blood specimens were drawn; whereas with the ward patients no such precaution was necessary, since the patients were already at rest in bed. Sera can apparently be stored in the ice box for at least two days without affecting the results of the test. Sera should be double centrifuged to avoid red cell contamination.

6. *Serum Dilution*.—The dilution of the serum in the test tube should be done exactly in the same way for both control and antigen sera. The solution should be added to avoid bubble or foam formation. Proper mixing should be done gently by rotary motion, to avoid foam formation and wetting the cork. (All corks should be thoroughly boiled several times, to extract the tannin that might precipitate the proteins.) Foam formation is permanent, since the proteins, such as the serum-globulin and serum-albumin, go into the surface and become altered in character so that they are not readily modified by acid or alkali.⁵

7. *Temperature of Incubation*.—A double boiler should be employed for heating the sera at 50° C. One cannot emphasize too much the precaution of keeping the temperature as fairly constant as possible, since a rise in temperature above 50° C.

is of more influence than heating at 50° C. for a longer time. It was found that heating a mixed serum for an additional one hour at 50° C. increased the drop number by 0.1 drop. In one experiment the control and antigen sera were heated at 65° C., with coagulation showing in the antigen serum in less than ten minutes, as indicated by increased opalescence of the fluid. It was found that the control serum was also markedly and equally affected with regard to increase in drop number.

8. *Vibration and Air Disturbances.*—It is obvious that a working spot should be selected where little or no vibration of the table top occurs. If necessary, a thick rubber sheet, or layer of cork or felt should be put under the stand which supports the stalagmometer. To avoid air disturbances, I employed a perforated watch glass cover, which set over the 50 c.c. beaker. The lower end of the stalagmometer was inserted through the watch glass for a distance of one-third the depth of the beaker. By this means, air currents were avoided and, in addition, the drop tended to form in an atmosphere fairly well saturated with vapor by the excess of the diluted serum not drawn up into the stalagmometer.

9. *Rate of Drop Formation.*—Du Noüy⁶ has shown that time is a factor in attaining equilibrium between the proteins in solution and those concentrating in the surface layer. He states, "Most of the values (surface tension) so far published correspond to an unstable state in the course of evolution toward the equilibrium and only happen to give approximately constant value when the instruments used in the case of hanging drop methods were identical and when the time required for the formation of a drop and its fall is about the same. The concordance of figures does not in any way imply the identity of the values of the tensions, except when, all things being otherwise equal, the time required in the formation of each drop is the same for a large number of drops." He further points out that in a serum of 1/100 dilution the surface tension, as expressed in dynes, is diminished by 2.5 dynes in the first minute. "According to whether a drop is formed in 10, 30, or 60 seconds, the value of the surface tension calculated from the drop weight will be somewhere on the curve between 66.5 dynes and 64.0 dynes." I have devised a new apparatus to permit a constant level of fluid in a portion of the stalagmometer so as to assure the same time requirement for drop formation for all of the drops. This work is reserved for a later paper.

APPLICATION OF MIOSTAGMIN REACTION

I. *Follow-Up Clinic of Radium-Treated Uterine Cancer* (Table II).—In this series of 64 cases, the miostagmin reaction was done on the same day that the patient was admitted to the hospital for examination. The reports of the follow-up clinic are those recorded for the examination of the patient on the same date that the test was made. In 45 cases, the test and the clinical condition of the patient agreed very well. Cases 10, 13, and 59 were borderline cases as far as the test was concerned and Case 30 would be classed doubtful, because of the presence of marked hemolysis in the serum. The positive result for Case 47 might be due to lipemia or a postoperative condition; Case 45 was postoperative; while Case 61 was due to lipemia, since the patient stated she had a very greasy breakfast. Cases 6, 42, 48, 54, and 56 might be explained as due to arteriosclerosis, as confirmed by results in Table III. Case 63 was a nephritic and also had a marked hypertension (260/100). The negative result for Case 33 agreed with the

TABLE II. FOLLOW-UP CLINIC OF RADIUM-TREATED UTERINE CANCER
(Woman's Hospital)

CASE NO.	AGE	DIAGNOSIS	RADIUM TREATMENT	REPORT OF FOLLOW-UP CLINIC	DATE OF TEST AND F-U. CLINIC	M. R. DIFFERENCE IN DROPS
1	56	Carcinoma of uterus (corpus)	9/20/23	Feels fine; no complaints; no bleeding	4/24/29	1.8
2	55	Carcinoma of cervix—Class III	3/15/29	Feels well; carcinoma shrinking; no slough present	4/24/29	1.6
3	45	Carcinoma of cervix—Class III	8/12/27	Feels well; discharge rather profuse; slough diminishing; fair result	4/24/29	2.1
4	42	Adenocarcinoma of sigmoid 6/7/28	2/16/29	Stomach gradually larger; constipated; fullness on left side	4/24/29	2.3
5	41	Adenocarcinoma of uterus—Class III	9/25/28	Clinically free from carcinoma	4/24/29	1.1
6	68	Glandular hyperplasia 5/20/21	6/4/27	Excellent health; no symptoms; no bleeding	4/24/29	2.6
7	54	Adenocarcinoma of uterus (fundus)	5/20/21	Very good health; uterus slightly enlarged; no evidence of any recurrence	4/24/29	1.4
8	60	Adenocarcinoma of uterus; adenomyosis-uteri; nephritis, chronic	4/16/26	Slight spotting; slight bleeding to touch in vagina	5/1/29	1.8
9	37	Carcinoma of cervix—Class III	6/17/27	No symptoms; uterus free; cervix contracted	5/1/29	1.2
10	61	Carcinoma of cervix—recurrent pyometra	3/30/28	Excellent condition; no discharge; no bleeding; clinically free from carcinoma; some pain in lower abdomen	5/1/29	2.0
11	61	Carcinoma of cervix (?)	11/1/27	Free from symptoms; no evidence of any recurrence of carcinoma	5/1/29	1.9
12	55	Involvement of stump—hysterectomy	8/5/27	Considerable discharge	5/1/29	2.5
13	56	Carcinoma of cervix—recurrent	3/19/27	Excellent health; no symptoms; no evidence of any recurrence	5/1/29	2.0
14	59	Carcinoma of cervix—Class III	2/24/28	Feels very well; no symptoms; normal condition of cervix and broad ligaments	5/1/29	1.9
15	40	Recurrent nodule in vaginal wall	6/5/28	Free from symptoms; pelvis clinically free from carcinoma; cervix healing and negative	5/1/29	1.7
16	55	Carcinoma of cervix (Group I—Memorial)	11/27/28	Slough diminishing	5/1/29	1.6
		Carcinoma of cervix—secondary	10/5/28			
		Carcinoma of vagina; anemia—secondary	2/1/29			

TABLE II—CONT'D

CASE NO.	AGE	DIAGNOSIS	RADIUM TREATMENT	REPORT OF FOLLOW-UP CLINIC	DATE OF TEST AND F.U. CLINIC	M. R. DIP-FERENCE IN DROPS
17	43	Carcinoma of cervix—Class III	11/ 2/28	No pain; slight slough present	5/ 1/29	1.9
18	56	Carcinoma of cervix—Class III	12/ 7/26	Considerable discharge; cervix free from carcinoma	5/ 1/29	2.4
19	56	Carcinoma of cervix—Class III	8/13/27	Excellent health; no complaints; no evidence of any recurrence	5/ 8/29	1.3
20	47	Carcinoma of cervix (Group I—Memorial) Class III	4/14/25	Some pain; no bleeding; margins of crater still active; considerable slough in crater	5/ 8/29	1.7
21	62	Carcinoma of cervix—Class III. Complete destruction of cervix	11/27/28			
22	60	Carcinoma of cervix—Class II	4/ 5/29	Feels well; no symptoms; no discharge or bleeding; no pain; excellent result	5/ 8/29	1.9
23	56	Carcinoma of cervix—Class III (Group II—Memorial)	9/18/25	Excellent general health; free from carcinoma; pain in hip	5/ 8/29	1.9
24	57	Thickening in cervix	11/21/25	Not making satisfactory progress; pain in back	5/ 8/29	1.4
25	55	Carcinoma of cervix—Class III (Group II—Memorial)	10/ 2/28	No bleeding; uterus normal	5/ 8/29	1.3
26	57	Carcinoma of cervix—Class III (Group II—Memorial)	3/ 8/29	Fixed mass appears at level of lower pole of left kidney; metastasis	5/ 8/29	2.5
27	51	Localized, small nodule	11/ 9/28	Feels well; cervix free from carcinoma; no evidence of nodule found which formerly was in vaginal vault	5/ 8/29	1.0
28	69	Recurrent nodule	11/16/28	No symptoms; feels fine; slight induration to broad ligament	5/ 8/29	1.6
29	60	Carcinoma of corpus uteri—glandular—Class III	7/17/28	Cervix negative for cancer	5/ 8/29	1.5
30	60	Adenocarcinoma of uterus	6/15/28	Excellent general condition; clinically free from carcinoma	5/ 8/29	0.7
			10/26/28	Appears much better; no complaints; gained 30 pounds; uterus freely movable—size of six months' pregnancy	5/15/29	2.1
			4/15/27			Marked hemolysis
			11/30/28			
			5/25/28			
			6/19/23			
			5/22/25			
			1/17/29			

TABLE II—CONT'D

CASE NO.	AGE	DIAGNOSIS	RADIUM TREATMENT	REPORT OF FOLLOW-UP CLINIC	DATE OF TEST AND F-U. CLINIC	M. R. DIFFERENCE IN DROPS
31	58	Carcinoma of cervix—Class III; syphilis	12/11/28	Feels well; no bleeding; no discharge; clinically free from carcinoma	5/15/29	2.2
32	41	Carcinoma of cervix—Class III	6/24/27	Feels well; clinically free from carcinoma	5/15/29	1.3
33	48	Carcinoma of cervix—Class III	11/15/27	(4/19/28—X-rays show metastases to lungs.)	5/15/29	1.6
		Induration in anterior lip	3/12/28	Feels much better; condition satisfactory		
34	43	Carcinoma of cervix; vesicovaginal fistula	11/10/27	Radiation not advised (5/29/29—local condition much improved)	5/15/29	1.6
35	52	Carcinoma of cervix—Class III	1/18/29	Feels well; no complaints; some pain on right side; no evidence of recurrence; clinically free from carcinoma below	5/15/29	1.9
36	43	Carcinoma of cervix—Class II	11/17/23	Feels well; no complaints; cervix is clinically free from carcinoma	5/15/29	1.4
		Uterus—carcinomatous	4/18/24			
		Recurrence on cervix	12/18/24			
		Parametria—involved	4/ 3/25			
		Pyometra—carcinoma of cervix—Class III	10/20/25			
		Recurrence—Class III	2/19/25			
37	69	Carcinoma of cervix—Class III	9/19/27	No bleeding; clinically free from carcinoma	5/15/29	1.3
38	47	Carcinoma of cervix—Class III	7/10/28	Cervix small, contracted; anterior vaginal wall involved, from cervix nearly to urethral orifice	5/15/29	2.5
		Nodule in left broad ligament	11/ 2/28			
		Involvement of anterior vaginal wall	5/24/28			
39	75	Carcinoma of cervix—clinically		(One month—postoperative); discharge moderate; good normal reaction for radium treatment	5/15/29	2.4
		Inflamed cervical tissue (Path. diag.)	4/ 9/29			
40	49	Carcinoma of cervix—Class III?	2/18/28	Clinically free from carcinoma	5/15/29	1.8
41	49	Carcinoma of cervix—Class III	2/ 7/29	No bleeding; complaint of white discharge; examination shows good progress in healing	5/15/29	1.8
42	61	Adenocarcinoma of uterus	7/27/28	No complaints; feeling much better; no evidence of recurrence of carcinoma	5/15/29	2.3
		(Complete hysterectomy 8/10/28)				
43	50	Carcinoma of cervix	2/14/22	Feels well; looks picture of health; examination shows perfect result; entire healing; no infiltration; no evidence of disease to be felt	5/15/29	2.0
		Crater about cervical canal friable, bled easily	8/25/22			
		Small mass in center of cervix bleeds to touch	2/ 9/23			
		Small bleeding spot—vault of vagina	12/16/24			Slightly hemolyzed

TABLE II—CONT'D

CASE NO.	AGE	DIAGNOSIS	RADIUM TREATMENT	REPORT OF FOLLOW-UP CLINIC	DATE OF TEST AND F-U CLINIC	M. R. DIFFERENCE IN DROPS
44	30	Carcinoma of cervix—Class II	1/18/27	No evidence of any disease; still complains of pain in hips	5/22/29	2.1
45	30	Vaginal discharge Carcinoma of cervix—Class III or IV Anemia, secondary	5/10/29 12/31/28	Improving in health; cervix gradually shrinking (tubes and appendix removed two months ago)	5/22/29	2.4
46	43	Carcinoma of cervix—Class III	2/7/28	Excellent health; no symptoms; cervix free from carcinoma	5/22/29	1.7
47	44	Carcinoma of cervix	11/17/21	In hospital one month ago for herniotomy; cervix free from carcinoma	5/22/29	2.8 Serum very turbid
48	67	Adenocarcinoma of fundus	9/23/27	General condition excellent; no bleeding; no evidence of any carcinoma	5/22/29	2.1
49	49	Endometritis, chronic Carcinoma of uterus Recurrence of carcinoma of cervix	11/7/27 1/4/29 3/21/29	Complains of backache; 5/29/29—complains of pain in back and rectum; cervix has shrunken down; no evidence of any recurrence; sound passed, small amount of fluid escaped	5/22/29	2.3
50	56	Carcinoma of cervix (Group II—Memorial)	10/2/28	Considerable pain in back; moderate slough; apparently responding well to radium	5/22/29	1.9
51	37	Carcinoma of cervix	3/8/29	Feels well; cervix contracting	5/22/29	1.7
52	55	Carcinoma of cervix—Class III	2/1/29 3/15/29	Free from spotting; feels much better; cervix is shrinking	5/22/29	1.6
53	40	Carcinoma of cervix; Wassermann +++ Vaginal discharge	12/15/22 2/27/23	Patient in excellent health; no symptoms; free from carcinoma	5/22/29	1.5
54	68	Adenocarcinoma of uterus (fundus)	4/16/26	No symptoms; feels very well; no evidence of recurrence	5/22/29	2.4
55	51	Carcinoma of cervix (inoperable) Carcinomatous tissue	7/12/29 12/6/19	Excellent health; free from carcinoma clinically	5/22/29	1.8
56	59	Extensive carcinomatous growth Adenocarcinoma of uterus (fundus) (Panlysterectomy 4/3/23)	4/16/20 6/23/22	In excellent health; no evidence of any recurrence of carcinoma	5/22/29	2.1

TABLE II—CONT'D

CASE NO.	AGE	DIAGNOSIS	RADIUM TREATMENT	REPORT OF FOLLOW-UP CLINIC	DATE OF TEST AND F. U. CLINIC	M. R. DIFFERENCE IN DROPS
57	47	Carcinoma of cervix	8/10/23	No symptoms; feels well; examination shows clinically free from carcinoma	5/22/29	1.8
58	43	Carcinoma of cervix—Class III	11/ 2/28	Cervix indurated (5/22/29); complains of pain in hips; involvement of right broad ligament	5/29/29	2.4
59	43	Carcinoma of cervix—Class II	10/11/27	Feels well; free from symptoms; cervix is irregular but soft	5/29/29	2.0
60	46	Carcinoma of cervix—Class III	12/10/26	Excellent health; no symptoms; cervix apparently free from carcinoma	5/29/29	2.4
61	54	Carcinoma of cervix—Class III Anemia, secondary	3/14/28	Excellent condition; cervix contracted	5/29/29	2.8 Very greasy breakfast
62	31	Metastatic carcinoma in peritoneum. Probably secondary to ovarian carcinoma; laparotomy 5/3/29	None	Pelvic examination shows cervix enlarged; frequency of urination due to carcinoma	5/29/29	2.5
63	41	Carcinoma of cervix—Class III; Anemia, secondary (heavy trace albumin in urine)	5/28/26	Free from symptoms; cervix is freely movable; apparently free from carcinoma	5/29/29	2.5
64	64	Adenocarcinoma of uterus (fundus) Watery, blood-tinged discharge Carcinoma recurrence in uterus	12/19/24 12/ 4/25 4/24/28	Had two small blood clots; considerable discharge; cervix moderately shrunken; slough present over it with discharge about it; advised to enter hospital	5/29/29	2.7

clinical report, but did not explain the metastases in the lungs. For Cases 20, 23, and 60, there was a marked disagreement between the clinical condition and the result of the test.

In conclusion, 6 cases gave a positive reaction which might have been due to arteriosclerosis or nephritis, and 4 gave an incorrect reaction which was not in agreement with the clinical condition. Considering these 10 cases as in complete disagreement between the test and clinical condition, we obtained about 84 per cent correct diagnostic tests. Further, if in the light of the results in Table III, one considers the 6 positive cases as explained by arteriosclerosis, then about 94 per cent of the tests gave fairly good diagnostic aid. The disturbing fea-

TABLE III. FEMALE CHRONIC CASES (MONTEFIORE HOSPITAL)

CASE NO.	AGE	BLOOD PRES-SURE	CONDITION	DATE OF TEST	M. R. DIFF. IN DROPS
1	67	180/ 92	Myocarditis; general arteriosclerosis; hypertension	5/24/29	3.4
2	78	166/142	Senility; general arteriosclerosis; hypertension	5/24/29	1.8
3	63	160/ 84	Hemiplegia; arteriosclerosis	5/24/29	2.0
4	67	160/ 80	Hemiplegia; general arteriosclerosis; hypertension	5/24/29	2.1
5	46	296/146	Hemiplegia; hypertension	5/24/29	2.6
6	66	250/110	Hypertension; general arteriosclerosis. Amputation leg (arteriosclerotic gangrene)	5/24/29	1.3
7	69	158/ 75	Arthritis; general arteriosclerosis	5/24/29	3.1
8	60	125/ 70	Arteriosclerosis; auricular fibrillation	5/24/29	2.5

ture, nevertheless, is that a negative result was obtained in 3 really positive cases of recurrence or continued presence of a malignant condition.

II. *Female Chronic Cases* (Table III).—This series of 8 cases was made as a control on those patients fairly well advanced in years and who gave a positive reaction, whereas the clinical condition was at variance with these positive results. Arteriosclerosis does give a high result of positive reaction very likely due to increased cholesterol content, but not all arteriosclerotic cases give a positive reaction. About 65 per cent of the cases gave a positive reaction, as due to arteriosclerosis.

III. *Surgical Ward Cases* (Table IV).—In the various conditions found among the 79 patients tested in the wards, 3 were classed as doubtful, since the miostagmin reaction equalled 2.0 drops, and 6 positive without explanation as far as our present knowledge is concerned—no leucocytosis, no milk injection, no transfusion, no post-operative condition, and no temperature elevation. Excluding the 3 doubtful cases, about 93 per cent of the cases gave a correct miostagmin reaction.

IV. *Pregnancy and Postpartum Cases.*—In the 10 cases tested in the prenatal clinic and in the ward, the miostagmin reaction, ranging from 2.7 to 4.1, was not only positive but was also on a much higher level than that listed for the malignant cases in Table II. Even after the evacuation of the uterus, the positive reaction persisted at least for a week. How early in pregnancy one can obtain a positive miostagmin reaction remains to be learned by further work.

V. *Sarcoma Cases* (Table V).—Three of the cases gave a negative reaction; 2 definitely positive without any known condition to explain

TABLE IV. SURGICAL WARD CASES (WOMAN'S HOSPITAL)

DIAGNOSIS	MIOSTAGMIN REACTION		
	POSITIVE	NEGATIVE	DOUBTFUL
Carcinoma of cervix	2		
Carcinoma of ovary	1		
Adenomyosis at tubal angle	1*		
Dermoid cyst of ovary	1*	1	
Myoma uteri	2*	16	
Benign polyp in fundus of uterus		1	
Cyst of ovary	1†	2	1
Salpingitis, acute	1		
Salpingitis, chronic		2	
Salpingo-oöphoritis, acute	4		
Salpingo-oöphoritis, chronic		6	
Tubo-ovarian abscess (no fever)		1	
Abscess of abdominal wall (no fever)		1	
Hyperplastic endometritis		2	
Prolapsed uterus		3	
Retroversion of uterus	1*	6	1
Cystocele and rectocele	1*	2	1
Laceration of cervix		3	
Erosion of cervix		4	
Vaginitis senile		1	
Postoperative cases with fever	5		
Abortion	4		
Retained secundines		1	

*Positive reaction unexplained.

†Blood transfusion on same day of test.

TABLE V. SARCOMA CASES (MEMORIAL HOSPITAL)

CASE NO.	SEX	AGE	CONDITION	DATE OF TEST	M. R. DIFF. IN DROPS	REMARKS
1	Male	27	Chondrosarcoma	5/27/29	1.8	Radium treatment 5/16/29
2	Male	19	Osteogenic sarcoma of femur	5/20/29	1.7	5th postoperative day
3	Female	39	Fascial sarcoma of leg	5/20/29	1.9	Radium treatment 5/19/29 to 5/21/29
4	Female	37	Osteogenic sarcoma of knee	5/27/29	3.0	Amputation 4/10/29. Coley's toxin, intravenously—5/25/29 and 5/27/29
5	Male	53	Neurogenic sarcoma of scapula	5/20/29	2.9	Normal temperature, but very weak condition. Expired one week later.
6	Male	59	Metastatic lymphosarcoma	5/20/29	3.8	5/20/29 Normal temperature; 84,800 leucocytes, 90 per cent lymphocytes

the positive reaction except by the character of the metabolism in these really bad sarcoma cases. Case 4 may have given a high positive result because of the intravenous injection of Coley's toxin. Nevertheless, we must disagree, as far as these few cases indicate, with Green's statement that the miostagmin reaction is always negative in sarcoma cases.

THE NATURE OF THE MIOSTAGMIN REACTION

Various investigations by different authors have been made to ascertain the nature of the miostagmin reaction. Some authors believed a new substance, formed during the pathologic process, reacted with the antigen to reduce the surface tension; whereas others thought there was an alteration of the chemical composition of the serum. Loeb⁷ advanced the belief that a change of degree of dispersion resulted when the serum was heated—through absorption by the micelle. Weis-Ostborn and Ehrentheil⁸ considered that the cholesterol content exerted an important influence upon the reaction; that a lowered cholesterol content of the serum produced a positive reaction, but that positive reactions could also be obtained with a high cholesterol content when this was partly obscured by the formation of globulin-cholesterol compounds (?). Calcium content of the serum seems to bear a direct relation to the surface tension as indicated by Sveila.⁹ The surface tension of carcinomatous sera ranged from 47.8 dynes to 55.2 dynes per cm.; whereas that of normal sera ranged from 62.6 dynes to 65.3 dynes per cm. The calcium content in carcinomatous sera varied from 0.142 mg. to 0.22 mg. per c.c.; while that in normal sera varied from 0.226 mg. to 0.246 mg. per c.c.

Because of the complexity of the serum content, we believe that several factors should be considered in attempting to explain the nature of the reaction. The P_H of the diluted serum with and without the antigen throws light upon the problem. In addition, from the miostagmin reaction results obtained in the pregnancy and abortion cases, it seems that an increase in cholesterol content does give a positive reaction, since the positive reaction is at higher level than that of carcinoma cases. One can also see a direct relationship of calcium content to surface tension, since the calcium would combine with the saturated fatty-acid (antigen) to form an insoluble soap. Another factor which seems to play an important rôle is the content of the serum-globulin and serum-albumin and their ratio. We see, then, that no one single factor accounts for the nature of the reaction. The following experiments and observations are offered in an endeavor to ascertain the nature of the reaction:

1. *Antigen Solution.*—The drop reading at 25° C. of distilled water, 0.85 per cent saline and antigen solution were respectively 54-6, 54-2, and 60-8. These were not previously heated. One sees at once that the very dilute solution of antigen in 0.85 per cent saline in itself gives a difference of 5.7 drops when the 0.85 per cent saline is used as a control.

2. *Cholesterol Content.*—It is of interest to note that a hypercholesterolemia has been found in arteriosclerosis, nephritis, nephrosis, dia-

betes, obstructive jaundice, in early stages of malignant tumors, and in pregnancy. These are the very same pathologic conditions in which a positive miostagmin reaction has been obtained. Mattick and Buchwald¹⁰ found a *higher cholesterol* content in plasma than in whole blood in 85 per cent of the patients with *cancer*, and a lower cholesterol content in plasma than in whole blood in 80 per cent of healthy patients. The results obtained in the arteriosclerotic cases as indicated in Table III seem to bear out the cholesterol increase as being the predominating influence in giving a positive reaction. Then, again, the high values obtained in the pregnancy cases seem to point to an increase of this constituent in the serum as contributing toward the high positive value. Finally, hemolyzed blood would give an increased cholesterol as well as protein content in blood serum.

3. *Serum-Albumin and Serum-Globulin.*—A very brief but interesting account is given by Robertson⁵ concerning the surface tension of protein solutions.

"The influence of dissolved protein upon the tension of air-water surfaces has been investigated. Gelatin, egg-globulin and hemoglobin diminish the air-water tension. The diminution is greater the higher the temperature. . . . The surface tension of gelatin solutions and *blood serum* is increased by the addition of small quantities of alkali and *diminished* by the *addition of small quantities of acid*. . . .

"According to Bottazzi, the surface tension of serum-albumin solution is at a maximum when the ionization is at a minimum. . . . The *maximum depression of the surface tension of water by serum-albumin* occurs at a reaction just on the *acid side of neutrality*. Undissolved protein does not affect the surface tension of water when shaken up with it. . . . The surface tension of a protein solution which is so electrolyte-free as not to coagulate on heating nevertheless diminishes on heating. This reduction of surface tension is reversible, for on standing for some time at ordinary temperature the solutions regain their original surface tension. . . .

"The surface tension of protein solutions diminishes during digestion."

(a) A determination of the P_H values of the saline, antigen solutions, as well as sera diluted, gave the following instructive values:

1. 0.85 per cent saline solution	P_H 7.35 Bromthymol blue
2. Antigen solution	P_H 4.2 Bromeresol green
3. Serum diluted with saline and heated 1 hour at 50° C. (4 sera tested this way)	P_H 7.75 to 7.95 Phenol red
4. Serum diluted with antigen solution and heated 1 hour at 50° C. (12 sera tested this way)	P_H 6.0 to 6.5 Bromthymol blue
5. One c.c. serum + 6 c.c. antigen solution + 3 c.c. saline. Not heated.	P_H 6.5 Bromthymol blue
Same heated 1 hour at 50° C.	P_H 6.55 Bromthymol blue
6. One c.c. serum + 9 c.c. antigen solution. Not heated	P_H 6.25 Bromthymol blue
Same heated 1 hour at 50° C.	P_H 6.30 Bromthymol blue

Serum plus antigen gives a diluted serum just on the acid side which in turn gives the maximum depression of surface tension. One notes

the increased alkalinity of the serum plus saline. The P_H of normal blood serum ranges from 7.3 to 7.5. Exposure to air would account for the higher P_H value.

(b) Now, upon heating the diluted sera, it was found that at 65° C. for one hour, the antigen diluted serum became very markedly opalescent, since it was on the acid side, while the saline showed very little opalescence, because it was on the alkaline side of neutrality. Furthermore, the surface tension determinations gave the value of 61 + 2 drops at 27.2° C. for the antigen diluted serum, and 61-1 drops at 27.1° C. for the saline diluted serum. The values were practically alike; the decomposition or denaturing had advanced to the same degree irrespective of the presence of the antigen.

(c) Of additional interest is the work by Chick and Martin¹¹ on the coagulation of 3 per cent hemoglobin solution.

TEMPERATURE	COAGULATION TIME IN MINUTES	CONC. HEMOGLOBIN
60.0° C.	90	13.5
65.6°	20	11.0
70.4°	6	14.1

The temperature coefficient of the process is very high and explains why it is so important to control the temperature of incubation of the diluted sera. It also has been demonstrated that peptids are found among the products of protein hydrolysis. Temperature and acidity are therefore important factors in lowering the surface tension of diluted sera.

(d) Another point of interest is that protein solutions are usually characterized by the possession of a high viscosity. We endeavored to establish some correlation of the results obtained in the antigen diluted sera (heated) as obtained with chronic female patients' sera (Table III) with those obtained by a sedimentation test carried out as follows: One c.c. of the antigen diluted serum was mixed with 1 c.c. of 20 per cent suspension of washed sheep's cells. Westergren apparatus was employed.

SERUM	MIOSTAGMIN REACTION	SEDIMENTATION AT 25° C. IN MM. AT END OF 2 HOURS
G. H.	3.4	4.0
M. R.	2.0	4.0
P. P.	2.1	4.5
B. C.	2.6	3.0
S. R.	3.1	3.8
A. D.	1.3	5.0
R. C.	1.8	3.5
E. V.	2.5	3.3
Antigen Sol.		4.0
Saline Sol.		3.7

No direct relationship was found to be present between the results obtained by the miostagmin reaction and those by sedimentation. Perhaps suspended red blood cells from the same patient might have given a correlation of results.

(e) It has been found that the surface tension of a mixed serum did not give the average of the individual determinations of the sera going to make up the mixed serum. It usually was lower and suggested some agglutination of the proteins, or else diminished dispersion of some of its constituents, particularly the serum-globulin and serum-albumin fractions. Coca¹² has suggested trying a mixture of sera of individuals in the same blood group to determine the influence of mixing on the value of surface tension.

(f) Of further interest is the fact that when a diluted caproic acid solution of the same concentration employed for the miostagmin reaction, but without the presence of saline, was added to the serum, it caused immediate turbidity and subsequent flocculation resulted after a short time. The flocculated material was found to be globulin. That not all of the globulin was flocculated was proved by the addition of saturated $(\text{NH}_4)_2\text{SO}_4$ solution to make a resulting one-half saturated solution, which caused additional globulin to be thrown out.

An experiment was performed to determine the influence of the absence of that amount of globulin thrown out by the diluted caproic acid. All the sera were heated for one hour at 50°C .

1.	} Serum + saline	56 + 9	} Difference = 2.4 drops
		58 + 17	
2.	} Serum + distilled water	56 + 4	} Difference = 1.3 drops
		57 + 10	

All the proportions were the same as in the regular determination for surface tension. The only difference was that in No. 2 the diluting solutions contained no saline but the concentration of antigen was, however, the same.

This experiment, we believe, indicates the importance of the globulin fraction in the serum in contributing toward the diminished surface tension of a serum when heated, particularly in acid solution. We are inclined to think that it is this fraction of the proteins that is easily altered as to its degree of dispersion even in the presence of saline.

SUMMARY

1. The miostagmin reaction may be a useful diagnostic aid to arrive at a fairly accurate diagnosis if used in conjunction with the clinical observations.

2. The miostagmin reaction may be of prognostic value, especially in radium-treated uterine cases, provided the clinical picture is also taken into account.

3. Contrary to statements in the literature, a positive miostagmin reaction may be obtained in very malignant sarcoma cases.

4. It is believed that the nature of the miostagmin reaction involves several factors, such as cholesterol content and calcium content as well as serum-albumin and serum-globulin content. The P_H of the antigen diluted sera, along with other experimental data, seems to indicate that the proteins and the ratio of their constituents (serum-albumin and serum-globulin) are of great importance in influencing the surface tension value.

The author desires to express his sincere appreciation for the material and co-operation given by Dr. George Gray Ward and his staff; also to Dr. James Ewing and Dr. B. S. Oppenheim for material obtained from their respective hospitals.

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Isbruch, F.: The Absence of Pathologic Organisms in the Uterine Cavity in Pregnancy. Arch. f. Gynäk. 135: 108, 1928.

The pregnant uterus is entirely free from pathogenic organisms until labor sets in. The occasional positive finding is usually due to faulty technic. Shortly after labor sets in, however, organisms wander into the uterine cavity and can be found even in the decidua and in the placenta. It must not be forgotten that the presence of such pathogenic organisms does not necessarily mean infection for the given organisms may not be pathogenic for the given patient.

RALPH A. REIS.

PSYCHOTHERAPY IN A GYNECOLOGIC SERVICE*

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MY SUBJECT is psychotherapy in a gynecologic service. Permit me at first to emphasize that to you as individuals and as a group, an exposition of psychotherapy in gynecology can be nothing new. Although psychotherapists for the most part maintain that gynecologic psychotherapy differs in no way from psychotherapy in general, you have always been well aware of the particular and peculiar importance of it in a sphere in which the function, maturation, use, cyclical changes, and atrophy are all so closely linked to profound psychic changes. Any disturbance in function could thus have an emotional value out of all apparent proportion. Also there would be a strong tendency to project any psychic or autonomic disturbance to the genital zone. However, I thought it might interest you to hear of the application of certain psychotherapeutic principles on an actual gynecologic service rather than a purely theoretical discussion of an ideal, or the attitude of a single exponent.

This work was started in the out-patient department of the gynecologic service at Mount Sinai Hospital about twelve years ago. At first, two hundred and fifty suitable cases were studied. For the last five years the work has been incorporated into the regular organization of the whole service. A separate morning clinic has been established to which borderline cases are referred, women in whom the symptomatology is not accounted for by the physical findings. Similarly, cases on the ward with a functional element are interviewed by a member of this clinic. The correlation between the in- and out-patient departments offers an opportunity for long term observation in the out-patient department of cases we have seen on the ward, and vice versa, the hospitalization and close observation and study of the concomitant and intercurrent organic disorders occurring in patients seen in the out-patient department.

The principles we have followed can be briefly outlined. All attempts to reduce the matter to a formula would probably result in half truths of descriptive value only. We have, however, tried to keep in mind, first, the concept of a patient as a biologic unit as opposed to an addition of organ systems. As a corollary of this, presenting symptoms are considered not only as to their bearing on the organic diagnosis, but as to their relationship to the dynamics of the life of the patient. (restated, this is to say, what value has this symptom

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for this patient; technically, what is the morbid gain?). The interplay of complex conditioned reflexes, the functioning of the sympathetic nervous system, the reciprocity of the internal secretory glands to the above and to each other, and the effects of thought and wishes on all of them have forced us to accept the possibility that in a given case a smaller or a larger fraction of symptoms may be psychogenic.

A second principle was that the diagnosis of a psychogenic etiology of all or of any residue of the symptoms was never to be made solely by exclusion. We did not consider it enough to search for organic causes and upon failing to find one, retreat to the diagnosis of neurosis or hysteria. Together with the diagnosis by exclusion, we looked for a *positive* demonstration of the presence of psychic factors. Of course, we attempted to exercise a stern self-critique in the quantitative evaluation, for no one has completely been spared psychic traumata and no two people bear them equally well. Eliciting such data required much time and some patience and careful listening by a trained observer. We found that the ordinary history very frequently fails to tell the truth as to possible psychic etiology, since the patient comes with the idea that her condition is organic. Without entering into details of the special method of taking a history in a case, I might summarize the instruction to interns and residents in its briefest form as follows: "Get the patient's confidence, invite the history, listen to the patient, and watch her while listening."

A third principle involved the acceptance of the possibility that both organic and functional determinants of the symptoms can exist side by side, be interrelated, prolong or increase each other's effects. The pain, for example, caused by an actual gynecologic lesion may persist after the lesion has been removed or corrected if this pain serves a valuable purpose to the unconscious of the patient. Vice versa, a constant mental preoccupation with a certain zone, chronic anger, fear, etc., can favor local tumescence and, for example, prolong the existence of a discharge.

A fourth principle was, that everything said or done be considered and weighed in terms of the interpretation given it by the patient. We have seen cases in which the failure to take this into account has kept patients in chronic invalidism.

We have felt that there were two jobs to do:

1. To differentiate between organic and psychogenic determinants.
2. To treat both. To the patient it makes no difference whether her pain or disability is of one or the other category, and it seems insufficient to dismiss the patient because the absence of organic ills precludes danger to her life.

The scope and purposes of this division are:

1. To weed out all psychotics and psychoneurotics and to limit to a minimum operative interference on such patients.

2. To aid in the setting of indications as to type of operative interferences. As an example of this one might mention the evaluation of the effect of tube ligation or castration, etc., on the subsequent life of a woman.

3. As supplementary psychotherapy in patients with a combined problem.

4. For the instruction of the younger men and postgraduate students in a broader approach to the patient as a whole.

5. Suggestive and reeducational, and in some cases radical psychotherapy in the treatment of functional disturbances.

The psychotherapy per se can be divided in two:

1. That subtle unlabeled psychotherapy that starts from the moment the patient is admitted and should continue without interruption until and even after the patient's discharge. Here I would like to say that I cannot lay too much stress upon the importance of the first or introductory words volunteered by a patient.

2. Specific psychotherapy, which is administered more consciously, is best done by men specially trained and continued after discharge from the ward. The particular school or particular label attached to it, whether it originates in Vienna, Zurich, Berlin, or Baltimore, matters little. For the most part it is not what the therapist says that counts as much as what the patient hears.

In the out-patient department we may more easily project our minds over a long period of time. In our special morning clinic for the study of frontier cases some men are being trained not to be over-enthusiastic in leaping to either an organic or psychogenic conclusion.

Though I have differentiated between psychodiagnosis and psychotherapy it is perfectly true that in many cases an attempt at psychodiagnosis will have a therapeutic value. The opportunity given the patient to tell her story completely in her own words, together with the sympathetic and complete attention of the doctor, not only gives valuable information, but permits the patient to get a perspective and an insight, with a high therapeutic value. We try to bear in mind that each patient presents to her doctor three intimately connected problems: the medical, the patient in relation to her body; the sociologic, the patient in relation to her environment; and the psychologic, the patient in relation to herself. Of the subdivision of the actual psychotherapy, I would like to discuss briefly the three main headings of adjustment, suggestive therapy, and radical therapy. (Please note that I use the term adjustment in a special sense, far more limited than the technical use of the word by mental hygienists.)

1. *Adjustment.* The patient and her environment are studied, her potentialities and the possibility of the situation are estimated. An im-

partial attitude is assumed and advice given in an attempt (a) to alter the environment to suit the patient, or, (b) to get the patient to accept the environment.

Brief example to illustrate this principle: A young woman with a chief complaint of dysmenorrhea and fainting spells had a negative gynecologic examination. Invited to talk freely, it developed that due to her husband's being out of work, she had to live with her in-laws, who made life miserable for her. She felt that she had reached the end of her rope and was developing a series of symptoms in defense. She was sent to the country through the cooperation of the social service department. Her husband secured a position, she moved from her environment, and her symptoms disappeared.

2. *Suggestive Therapy.* This we have used in the form of (a) authoritative treatment, firm when the patient needs to lean on authority. It may be accompanied by definite commands or instructions and we feel that upon such suggestion rests the efficacy of many medicinal and manipulative treatments. The use of pessaries, cautery, tampons, etc., often have a purely suggestive beneficial value which seems legitimate in therapy as long as the doctor is conscious of what he is doing and why. (b) Gentle treatment. In such instances the patient is a child who wants and needs a mother (the sex of the gynecologist does not matter here).

We have not used hypnosis in hospital practice in spite of its undoubted value in some cases, for a number of reasons. It requires very special skill, it has inherent dangers in cases bordering on psychoses. In many cases its effects are very temporary, and it carries an aura of undeserved disrepute, widespread among both the laity and the profession. It differs from suggestion in degree rather than in kind.

The results of suggestive therapy in such conditions as pruritus vulvae, dysmenorrhea, pelvic pain, etc., are usually only temporary. The nasal cautery treatment for instance, relieves dysmenorrhea in a large percentage of cases, but the relief lasts through two periods on the average. This fact has strengthened our belief that it is purely a suggestive therapeutic procedure.

3. *Radical Psychotherapy.* In radical psychotherapy we attempt to remove the cause of the mental difficulty by either a rapid or a slow method. The choice of which, and the distinct limitations of each, are determined by the intelligence of the patient, her social status, her cultural resources, her moral fiber, the type of physician, the time at his disposal, the severity of the situation, and the definitive diagnosis.

To illustrate one of these factors, it may be important in one case to stop all medication and treatment in order to fully impress the patient with one's conviction as to absence of organic disorder, and in another to insist on some routine treatment or topical application of pessary changing, to insure regular observation until the suggestions or re-education have been adequately absorbed.

I shall give two examples in skeletonized outline illustrating the rapid and the prolonged type of radical psychotherapy:

A young woman complained of pain in the left breast; she had been to a doctor, who assured her there was nothing wrong. She was not satisfied. Examination of the breast, the heart, the whole woman was negative. (Here I may add that wherever a functional disturbance is suspected we feel that the indication for thoroughness in physical search is quadrupled.) I then asked what member of her family had cancer of the breast. She said, "My sister died of it and I have had my pain since." Then, knowing how often a cancerphobia is a symptom of a neurosis revolving about sterility, it was determined that her sister had had two children—the patient had none. She was envious of her sister and had identified herself with the sister. (I am simply giving a sufficient outline of the facts to indicate the trend.) She was then abruptly told that the real reason for her visit was sterility. The response was remarkable. "How did you know that I was going to talk to you about that, etc." The pain in the breast disappeared. Her sterility is being studied. In this case, the particular method of imparting to her the mechanism, with its touch of the dramatic, drove home the point with a valuable emphasis, and one brief interview was enough.

In the majority of cases it seems not only unnecessary, but unwise, to become involved in elaborate theoretical discussions with the patient in respect to mechanisms of the unconscious. Practical psychoanalysis, and for that matter practical psychotherapy, in general, are quite different from their theory. Let me put it in this way—the theory the physician should master and use *for* the patient and not *with* the patient. Illustrative case, radical therapy, prolonged treatment.

A woman of twenty-seven complained of severe dysmenorrhea as well as fainting spells, insomnia, attacks of nausea. Physical examination showed no local lesion, but did show a severe tie that she had had for twenty years. This had been diagnosed as chorea. Now, no chorea lasts for twenty years. A long conversation showed that this tie interfered with everything that the young woman might want to do—study, work, dance, marry, and so on. Her entire character had been warped and from my interviews with her relatives, I ascertained that we were dealing with a worth-while person suffering from a severe personality disturbance. A prolonged course of reeducational psychotherapy was recommended with the result that she became an efficient, attractive, sociable girl, minus the tie and minus the dysmenorrhea, incidentally. Please note that it was only incidental, as the initial diagnosis was that of a neurosis far more important to tackle.

Some of the symptoms we have frequently found to be functional are dysmenorrhea, irrespective of the position of the uterus, dyspareunia, vaginismus, frigidity, vague pelvic pain, excessive menopause symptoms, pruritus vulvae, tender ovary, backache, a feeling of protrusion in the absence of prolapse or cystocele, leucorrhea without pus and occasionally with pus, pains under the left breast associated with a sensation of something moving around in the abdomen, frank pseudo-cyesis, some cases of urinary frequency or urgency with clear urine and negative cystoscopic findings, some cases of incontinence of urine,

obstinate constipation, and some cases of amenorrhea and menorrhagia. Occasionally cases of irregular bleeding have been shown to belong to this group; on the whole this is unsafe teaching, however. It is true that under the influence of fright, from a contemplated vaginal examination or a set wedding date a premature period may occur, but on the whole in any case of metrorrhagia, we must have faith in a diagnostic curettage, even if the overwhelming majority of our pathologic reports read hyperplastic endometrium.

How far one goes in the direction of attributing these various symptoms to psychic causes will vary considerably. It has been the experience of the men who have worked most in this field that the more one investigates along this line the larger the variety of symptoms that have been found possibly due to functional disturbances.

One other thing—what has psychoanalysis to do with gynecologic psychotherapy? Let me emphasize that the term psychoanalysis refers to three distinctly different things. One, a formal, elaborate, long, difficult, psychotherapeutic method, one of a number of psychotherapeutic methods applicable to a small minority of mental cases. It should be done only by a well-trained man who has himself been analyzed and should not be accompanied with treatment for an organic ill at the hands of the same physician. The treatment precludes an advisory rôle, so if you hear that an analyst has advised this or that, you will know, either that you have been misinformed or that no real analysis has been done. At this point I would like to warn against the use of psychoanalysis in its many modified forms by untrained persons. Like any potent medicine that has the possibility for good, it has the possibility for harm, and anyone who does not understand thoroughly the divers manifestations of transferences and resistance will get into difficulties.

A second meaning of the term psychoanalysis as generally used is a body of knowledge acquired by means of psychoanalytic investigations and research, roughly grouped under the term "psychology of the unconscious."

The third definition of the term refers to a technic for investigating the mind which enlarges the armamentarium particularly in taking a history. Although the formal psychotherapeutic procedure is used practically rarely the passive modest utilization of information obtained in the interest of the patient through the knowledge of the principles, often proves valuable.

Permit me to mention one type of treatment showing the application of certain principles of the dynamics of a psychoanalytic cure in a nonanalytic treatment of dyspareunia and vaginismus. The treatment begins with the interdiction of all attempts at coitus. The physician then listens attentively and sympathetically with the fewest possible

words of interruption to the entire story with all its trimmings, including everything the patient is reminded of in her experience or fantasy. During this time the patient gets to like her physician. This is followed by a very brief and very gentle examination. The vaginitis is treated and this is followed by the gradual employment of a small speculum. The speculum is replaced subsequently by a test tube the size of which is gradually increased. The patient is then instructed to introduce the largest test tube herself. After this an explanation is given to the patient of what has transpired during the treatment, how her confidence in the physician has overcome her defense spasm. Then comes an interview with the husband, which includes the fullest discussion of his technical and psychologic approach. Then the patient is dismissed from further treatment or recommendation before coitus is attempted. In an analytic cure, the neurosis is converted into an analytic neurosis, and the patient then cured of that. In this case, analogously, the fear is converted into a medical fear, of which the patient is cured, to go out into the real world to reconvert and profit from it, the polarization now toward her husband.

I could, but need not, for this audience enlarge upon the importance of the sequence of events, the establishment and subsequent constructive displacement of the positive transference and the rôle of self-introduction of the large glass test tube.

The training advantageous to men who are interested in the organization of such work would include a certain amount of psychiatry and acquaintanceship with modern psychotherapy, knowledge of the resources of medical gynecology as aids in suggestion, knowledge of sex hygiene and the more common forms of sexual difficulties and incompatibilities, the possibilities and limitations of psychiatric social service work and a working knowledge of contraception and contraceptive problems.

We have availed ourselves fully of the closest cooperation with other departments of the hospital, particularly the departments of neurology and psychiatry, the mental health class and the social service departments. It might conceivably be argued that the availability of these departments would be sufficient to obviate the necessity, or discount the value of such work done within our own department. We have not found that to be so because of:

1. The very large number of such cases.
2. The tendency toward limitation to an organic approach by the neurologic department.
3. The tendency toward an excessive emphasis on psychogenic factors by the mental health department.
4. The perspective obtained by a worker in both fields.

In general it seems that the work has had the following results:

1. It has helped to limit and to clarify operative indications, eliminating almost entirely certain types of operation.
2. It has stimulated men in contact with the work on the wards in the direction of a new viewpoint.
3. It has done something quite specific for a group of patients who would otherwise have been left more or less to their own resources after having been diagnosed as neurotic.
4. It has given those who have spent their time in the investigation ample reward in the increased understanding of their patients, an increased tolerance of their oddities and an increased respect for the complexity of the whole psychophysical apparatus.

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(For discussion, see page 430.)

Skajaa, K.: Cessation of the Coagulation of Blood in Postpartum Hemorrhage, "Shock Bleeding." Acta obstet. gynec. Scandinav. 9: 453, 1930.

In 13,000 confinements, Skajaa found 11 cases of postpartum hemorrhage in which the blood coagulated normally during labor. However, coagulation time was found to be fifteen to twenty minutes or longer, after the bleeding had ceased. When flow again started the blood did not coagulate at all. In 7 patients the uterus was firm and in 2 patients it was completely atonic. In all the patients there had been a preliminary abundant hemorrhage and in all but one there had been intrauterine manipulation. There were 4 cases of placenta previa and 3 of abruptio placentae. In most instances the bleeding began with noneoagulation of the blood and a change in the patient's condition resembling obstetric shock.

The uterine blood did not coagulate because it lacked fibrinogen. Blood taken from a vein coagulated in a normal manner. The uterus was the seat of a local hemophilia. The author believes that shock is the basis of this type of hemorrhage. The only way to treat this condition successfully is by vaginal hysterectomy. In 7 cases death occurred from hemorrhage. Four patients recovered after massive transfusions.

J. P. GREENHILL.

TRICHOMONAS VAGINALIS VAGINITIS IN PREGNANCY*

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THE occurrence of *Trichomonas vaginalis* in the secretion of the vagina in the pregnant as well as in the nonpregnant woman has been reported by a number of European authors in recent years. Only a few investigators in this country; namely, DeLee,¹⁶ Greenhill,²⁸ and C. H. Davis,¹³ have made a clinical study of this interesting flagellated organism. Its morphology has been studied by several protozoologists, notably by Hegner.³¹ Although Donné²¹ first described *Trichomonas vaginalis* in 1836, very little is definitely understood concerning its life history, morphology, transmission, and pathogenicity.

The presence of persistent abnormal vaginal secretion, leucorrhea of various types, and definite vaginitis in the pregnant woman led us to an investigation of the possible etiologic factor responsible for these conditions. The discovery of actively motile *Trichomonas* in fresh smears of the vaginal secretion of pregnant women directed our attention to this organism as a probable underlying cause. The present study was further undertaken because considerable doubt prevails concerning the pathogenicity of this flagellate. The material for the investigation was obtained from patients attending the antenatal clinic of the Jefferson Medical College Hospital. The morphologic study was made by Dr. David H. Wenrich, Professor of Zoology at the University of Pennsylvania.

Donné discovered this flagellated protozoön in the vaginal secretion and named it *Trichomonas vaginale*.

The incidence of *Trichomonas* in the vaginal secretion has been variously reported by numerous authors. All of the writers have observed this protozoön in the yellowish, cream-like, and markedly acid secretion of pregnant and nonpregnant women. In 1855 Koelliker³⁸ and a few years later Haussmann³⁰ found the parasite in from 40 to 50 per cent of gravid and nongravid women. Hoehne³³ noted the flagellate in the vaginal secretion of 34 per cent of 102 pregnant and in 28 per cent of 104 nonpregnant patients.

In 1913, Brumpt⁸ found the parasite in 10 per cent of women in a gynecologic clinic in Paris. Wille⁷¹ noted the organism in 40 per cent of women complaining of leucorrhea.

In recent years, Seitz⁶¹ reported the flagellate in 20 per cent of pregnant women; Traugott⁶⁶ in 50 cent of nonpregnant women; Reuling⁵⁸ in 18.4 per cent of women with leucorrhea; and Ponoschina⁵² in 16 of 29 adults manifesting profuse vaginal

*Read at a meeting of the Obstetrical Society of Philadelphia, May 1, 1930.

discharge. Flaskamp²⁵ found that only one-third of the patients with *Trichomonas vaginalis* complained subjectively.

In 1928, Davis¹³ and Greenhill²⁸ diagnosed and treated *Trichomonas vaginalis* vaginitis in 38 and 56 private patients, respectively. M. N. Andrews² recently found the organism in the vaginal discharge of 20 per cent of 100 women studied in England.

A flagellate apparently morphologically similar to the *Trichomonas* observed in the vagina, has also been observed in the urine of individuals of both sexes. K nstler,³⁹ in 1883, was seemingly the first to mention finding this organism in freshly voided urine. The first undoubted case of *Trichomonas* infection of the urinary tract of man was reported by Marchand⁴⁹ in 1894. Since then a number of writers; namely, Dock,¹⁷ Miura,⁵⁰ N. S. Davis,¹⁵ Arnold,³ Rasmussen,⁵⁶ Lewis and Carroll,⁴¹ Dastidar,¹² C pek,¹⁰ Visser,⁶⁸ Seitz,⁶¹ and Flaskamp²⁵ have reported the occasional presence of this flagellate in the urine of both the male and female.

CULTIVATION

Several methods have been recommended for the cultivation of *Trichomonas vaginalis* by workers who have cultured the organism with varying results. The media are generally similar, containing for the most part saline with nutrient material, such as fresh or dried serum or ascitic fluid. Lynch,⁴⁶ in 1915, was the first to cultivate the parasite with any degree of success, obtaining a growth in beef broth.

The most satisfactory results, however, have been secured with Loeffler's blood serum, diluted with citrated saline to which is added a small amount of fresh egg albumen to inhibit the rapid growth of bacteria. This combination was first used to cultivate various trichomonads by Tanabe⁶⁴ and Cleveland¹¹ in 1925. The composition of the medium, as used in the present investigation, is as follows:

Loeffler's (dehydrated) blood serum	0.5 gm.
Sodium chloride	0.7 gm.
Sodium citrate	1.0 gm.
Distilled water	100 c.c.
Egg albumen	5 c.c.

The medium is prepared in the following manner: The sodium chloride and sodium citrate are boiled in distilled water for ten minutes and allowed to cool. Loeffler's dehydrated blood serum is then added. This solution is citrated to P_H 7.6, and 5 c.c. of fresh egg albumen added. To maintain the protozoa free as possible from bacteria, the medium is then tubed and sterilized by the fractional method in the Arnold sterilizer at 90° C. for one hour daily for three days. A sterile tube of the medium is always available to receive the material collected from the patient in the following manner: A vaginal speculum is inserted without employing a lubricant, exposing the cervix to view. Using the lower blade of the speculum as a spoon, an effort is made to scoop up as much secretion as possible from the lake usually present in the posterior fornix and from the vaginal wall itself. This is transferred to a sterile tube containing one or two cubic centimeters of normal salt solution. A drop of the material is then examined under high power for living flagellates. The saline-secretion mixture is then poured into a tube containing the saline-citrate-serum solution and incubated at 37.5° C. The cultures are examined twenty-four hours later. Subcultures are made from all those showing a growth while those not showing any live organisms are permitted to remain in the incubator for twenty-four hours longer. If no growth appears at this time,

the tube is discarded. Since the trichomonads grow at the bottom of the tube with the bacterial sediment, it is necessary to withdraw the specimens from the precipitate with a capillary pipette for examination and for transfer to new tubes.

In the present investigation, cultures were prepared in the manner described from the vaginal secretion of all patients with positive smears. The organisms from 45 patients were successfully cultivated, subcultures being made daily. The cultures were preserved or maintained for five or six days and then discarded.

Smears were also made either from the secretion directly or from the preliminary saline mixture in all positive cases and fixed immediately in Schaudinn's sublimate alcohol. Each smear is fixed for fifteen minutes. It is then transferred to 50 per cent alcohol for twenty minutes and finally placed in 70 per cent alcohol where it remains until stained with Heidenhain's hematoxylin.

MORPHOLOGY AND LIFE HISTORY

The morphology of *Trichomonas vaginalis* has been presented by a number of writers since the original account given by Donné (1837), notably by Bensen,⁵ in 1910, Reuling (1921), and Hegner (1925). All these later observers agree on the general features of organization of this flagellate, but there is some disagreement as to details.*

The only method of reproduction that has been observed in this study is binary fission, with details which parallel those recorded for other species of *Trichomonas*.

So far as the present observations permit of an opinion, it would appear that the characters already described for *Trichomonas vaginalis* serve to distinguish it from all other species of the genus. This is important in view of the fact that this is the type species of the genus and in view of the as yet unsolved problem of transmission from host to host. Although stool examinations have been made from only 4 of the patients positive for *Trichomonas vaginalis*, these were all negative for intestinal trichomonads. Therefore, an origin from some other source than the intestine is indicated for *Trichomonas vaginalis*.

CLINICAL OBSERVATIONS

Specimens collected at various times from 300 pregnant patients registering in the antenatal clinic revealed the presence of trichomonads in 61, or 21 per cent (Fig. 1). The actively motile flagellates were usually associated with many leucocytes, bacteria, and squamous epithelial cells. That the organism is a more common invader of the vagina of colored women is disclosed in Fig. 2. It is noted that 54, or 32 per cent, of the 164 colored patients showed *Trichomonas*, as com-

*See articles in this JOURNAL by C. H. Davis, Vol. xviii, pp. 196, 575, and J. P. Greenhill, Vol. xvi, p. 87, also an article to be subsequently published by the author.

pared with 13, or 9.5 per cent, of 136 white patients. The marked variance in the percentages may be attributed to differences in the local hygienic condition.

Only 8 (13 per cent) of the patients with *Trichomonas* infection complained of local symptoms. Many others, however, on being closely questioned in this respect usually mentioned the existence of a profuse irritating or burning, yellow or white discharge. The vaginal secretion was materially altered in practically every instance from the usual milky white material, consisting of mucus and epithelium, to a

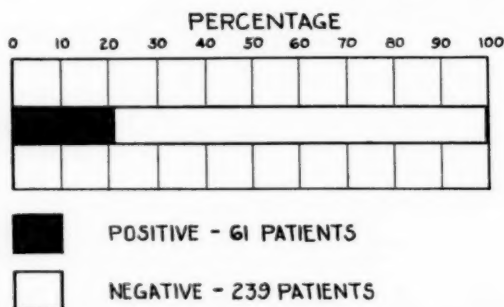


Fig. 1.—Incidence of *Trichomonas vaginalis* infection in three hundred pregnant women regardless of race.

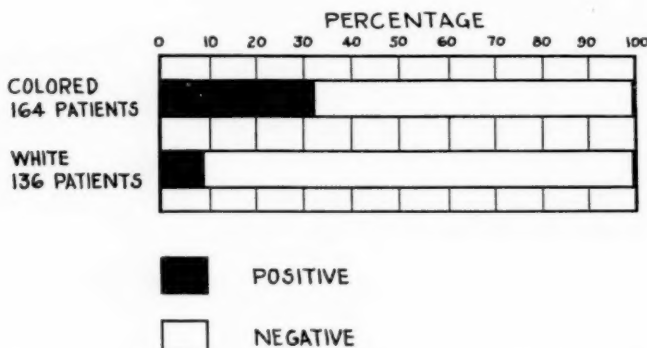


Fig. 2.—Incidence of *Trichomonas vaginalis* infection in three hundred pregnant women according to race of patient.

thick seropurulent, creamy yellow, and often bubbling or foamy discharge, containing numerous bacteria, trichomonads, and leucocytes. Several patients complained of pruritus and chafing in addition to profuse leucorrhea. On examination the external genitalia usually showed purulent discharge exuding from the introitus. The inflammatory phenomena ranged from a diffuse reddening of the vaginal wall and vestibule with frothy purulent discharge below the cervix to a more or less extensive intertrigo of the vulva and surrounding area. In severe cases the appearance of the vagina resembled (with the exception of the frothy character of the secretion) that of an acute

gonorrheal vaginitis. However, in none of the patients studied was the gonococcus an accompaniment, though a few authors (Loeser,⁴⁵ Flaskamp,²⁵ Seitz,⁶¹ and Gragert²⁷) have observed this dual infection. Hoehne, on the contrary, states that he has never noted the combination of gonorrhea with vaginal trichomoniasis.

TREATMENT

Several methods of treatment have been advocated which have for their aim either a biologic alteration of the bacterial flora or a destruction by chemical means of the *Trichomonas* itself. Regional prophylaxis should be practiced by proper cleansing of the anal region after defecation, although it has not as yet been determined with certainty that the intestinal tract is the source of the infection. Vigorous and repeated treatment is usually required before the vaginitis is relieved and the vaginal mucosa permanently freed of the parasite. The following plan of therapy has proved successful in the majority of cases: The anal region, vulva, and vagina are first thoroughly scrubbed with tincture of green soap, followed by sterile water, and then washed with 1 per cent compound cresol solution. The vagina is then dried with cotton pledgets and a tampon saturated with boroglycerin (10 per cent) is inserted and allowed to remain overnight. Hoehne recommends gelatin capsules containing 3 c.c. of the borated glycerin to be filled immediately before using and inserted by the patient herself. A 0.5 per cent lactic acid douche is prescribed daily for several weeks in order to reestablish the normal bacterial flora. The employment of a culture of organisms similar to the lactic acid bacillus has also been suggested (i.e., Bacillosan recommended by Loeser). This, it is claimed, disinfects the vagina biologically and promotes the growth of the selected organism which is antagonistic to other forms of germ life. Finally, the most important aspect of the therapeutic plan is found in vigorous mechanical cleansing.

Tampons of methylene blue have been used successfully by Greenhill; while DeLee has secured good results with glycerin and sodium bicarbonate tampons. The use of drying powder, such as kaolin, has also been recommended.

DISCUSSION

Many attempts have been made to determine directly whether *Trichomonas vaginalis* is the actual exciting cause of the colpitis or the leucorrhea with which it so frequently is associated. At the present time, no one has been able to prove conclusively that it is pathogenic, although this is the consensus of opinion among those who have observed and treated purulent vaginitis and persistent leucorrhea existing without apparent cause. Nevertheless, several workers among whom may be mentioned: Haupt,²⁹ Seeliger,⁶⁰ Loeser,⁴⁵ Füh,²⁶ and

Wolfring,⁷³ maintain that this parasite is only a harmless inhabitant of the vagina and not in the least pathogenic. Haupt insisted that the organism is nonpathogenic because the transmission of *Trichomonas* from the vaginal secretion to a normal woman failed to produce any inflammatory reaction or any changes in the character of the vaginal secretion, although large numbers of the flagellates were present.

An array of clinicians considers that *Trichomonas vaginalis* has a definite pathologic significance. DeLee, Greenhill, and C. H. Davis speak of *Trichomonas vaginalis* vaginitis as a specific entity; moreover, a larger group of authors in Europe has pronounced this organism as the factor in the causation of this condition.

Seitz and Hoehne contend that the parasite is often pathogenic in nature and that it also tends to increase the virulence of the bacterial flora in the vagina. The latter author was the first to associate this organism with purulent vaginitis, the strongest proof of his assertion being the fact that the organisms were so numerous in the pathologic discharge and that the vaginitis subsided as the trichomonads disappeared.

A definite vaginitis; i.e., subjective plus objective symptoms, was present in only 13 per cent of our series of patients, whereas almost all possessed an abnormal type of vaginal secretion. In our opinion *Trichomonas vaginalis* is not a harmless invader of the vagina but is pathogenic and under proper conditions; i.e., in association with other organisms, is capable of producing an inflammatory reaction exciting a pathologic exudation or discharge containing numerous leucocytes, and culminating occasionally in a pronounced vaginitis.

Several authors (Schmid, Kamniker, Liss and Gragert) have investigated the effect of *Trichomonas vaginalis* infection in pregnancy on the puerperal morbidity rate. These authors agree that the presence of a vaginal infection with this organism in pregnancy greatly increases the danger of puerperal infection. The puerperal morbidity rate of patients manifesting a *Trichomonas vaginalis* vaginitis antepartum was considerably greater than in those who did not exhibit this condition. It is as yet impossible to make any statement regarding the morbidity rate in our series of patients since only a small proportion of those studied have been delivered to date.

SUMMARY AND CONCLUSIONS

1. *Trichomonas vaginalis* was found in the vaginal secretion of 61, or 21 per cent, of 300 gravid women examined.

2. The morphology of the organism is briefly described. It is usually pear-shaped and ranges in length from 7 to 30 microns, while the width is usually one-half to two-thirds of the length. A slender axostyle projects posteriorly, four free flagella project anteriorly,

and an undulating membrane extends from the anterior end backward along the surface to about the middle of the body.

3. The parasite is a more common invader of the vaginal tract of the colored woman, being found in 54, or 32 per cent, of 164 colored patients; and only in 13, or 9.5 per cent, of 136 white patients.

4. Eight, or 13 per cent, of the patients with vaginal trichomoniasis complained of local symptoms.

5. Vigorous and repeated mechanical cleansing is the most important step in the treatment of the vaginitis associated with this parasite.

6. Finally, it is our belief that under suitable conditions the organism may assume pathogenic proclivities similar to other organisms, or in association with bacteria, may give rise to serious local or ascending infection of the genitourinary tract, particularly in the puerperium.

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1717 PINE STREET.

(For discussion, see page 438.)

Solms and Klopstock: The Pregnancy Test of Aschheim and Zondek and Its Significance in the Differential Diagnosis of Amenorrhoeic and Climacteric Disturbances. Deutsche med. Wehnschr. 55: 1919, 1929.

The authors report highly satisfactory results with this test in diagnosing pregnancy. There was practically no failure when the test was performed later than the eighth day after the missing menstruation. In a few cases a weak positive test could be obtained as early as three days prior to the expected menses. In the few cases in which the test erroneously was pronounced negative, the findings on dissection of the test animal were at least so dubious as to suggest the necessity of a check. On second trial all these urines gave finally a correct positive reaction.

The authors extended the application of this test for the differentiation of two types of amenorrhoea and climacteric disturbances. Either condition is considered to be a dysfunction of the hormonal system with either hyper- or hyposecretion. By dividing the urine into a heated and nonheated portion the test can be further elaborated for the differentiation of ovarian and pituitary hormones as the latter will be destroyed by higher temperatures. Four cases are cited in order to demonstrate the possibility of discovering different and adverse hormonal concentrations in the urines of patients suffering from those conditions and the satisfactory therapeutic results derived from this refined diagnosis.

G. E. GRUENFELD.

STUDY OF NEONATAL DEATHS OCCURRING IN 6000 CONSECUTIVE DELIVERIES*

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A FEW years ago, a series of statistical studies was undertaken on the Obstetric Division of the Woman's Hospital, in the hope that these studies would reveal some helpful information. At that time analyses were made of the maternal deaths¹ and of the stillbirths.² These were based on the same 4000 consecutive ward deliveries, and covered a period of seven and one-half years (June 26, 1919, to January 1, 1927). The present work supplements these and is an analysis of the neonatal deaths occurring in the same 4000 consecutive deliveries to which have been added 2000 more deliveries making a total of 6000. This brings the study up to the present time and covers a period of about eleven years (June 26, 1919, to June 7, 1930).

In this series we have classified as neonatal deaths all cases in which the baby breathed after delivery, even though the respirations were feeble. Babies who were born with hearts which were beating, but who never breathed, have been considered stillbirths. Twenty-eight weeks of gestation have been accepted as the period of viability and any baby born alive before the twenty-eighth week, and subsequently dying, has been excluded. All deaths have occurred before the babies were discharged from the hospital, and with very few exceptions have occurred within the first two weeks following delivery. On this basis there have been 117 neonatal deaths among babies born to 110 mothers, or 17.83 per 1000 delivered mothers. Eleven of the deaths have been in twin pregnancies; in 5 cases both twins died, in 5 cases one twin died, and in 1 case one twin died and one was a stillbirth. There was one mother who had triplets, all of whom died. The length of time these babies lived has varied from five minutes to thirty-seven days. However, only 6 babies lived more than fourteen days. Fifty-one out of the 117, or 43.41 per cent, died during the first twelve hours after delivery.

The majority of these mothers, 91 of the 110, registered in the prenatal clinic, generally between the third and sixth months, and 19, or 17.27 per cent, were emergency cases; i.e., patients who came to the hospital for the first time, when in active labor or when suffering from

*Read before the New York Obstetrical Society, October 14, 1930.

some serious complication necessitating hospital care. There were in all 14 cases of toxemia; 9 among the prenatal cases, and 5 among the emergency cases, an increased incidence among the cases which were not attending the prenatal clinic.

Wassermann tests were made on 89 of the patients. Four had positive Wassermanns. None of the babies from the four plus mothers showed clinical signs of lues. In 2, however, the cord Wassermann was positive. In the other 2 the cord Wassermann was not taken. The 21 not having Wassermann tests occurred very early in the series.

Prematurity was a frequent complication in this series of neonatal deaths, there being 58 babies born before term. In 42 cases the cause of death was *directly attributed* to the prematurity. Fifty of the premature cases went into labor spontaneously and 8 were induced. Toxemia was associated with prematurity in 10 instances, syphilis in 1, premature separation of the placenta in 1, twins in 11 cases, triplets in 1, influenza in 2, placenta previa in 3, polyhydramnios in 2, congenital anomalies in 4, and pyelitis in 1 case.

TABLE I

28 to 30 weeks	14
30 to 32 weeks	18
32 to 34 weeks	13
34 to 36 weeks	8
36 to 38 weeks	5
38 to 40 weeks	59
	<hr/> 117

In this group of cases, contrary to our first impression, the number of babies delivered normally and abnormally was about equal. Fifty-five of the 117, or 47.18 per cent, were delivered without operative interference.

TABLE II

Normal	55
Forceps	
Low	16
Medium	8
High	3
Breech	16
Breech after version	15
Vaginal cesarean section	1
Cesarean section	3
	<hr/> 117

TABLE III

Normal	86
Flat	9
Justominor	6
Atypical (high promontory)	2
Not measured	7
	<hr/> 110

Pelvic deformity in the series of neonatal deaths, as in the series of stillbirths, was not an important factor. Eighty-six of the patients, or 76.36 per cent, had a normal pelvis, while 17 had an abnormal pelvis, and 7 were not measured. This is indicated in Table III.

Sixty-seven babies were autopsied and 50 were not. Among those autopsied, intracranial injuries were found in 25 babies; 7 of these were delivered normally, and 7 by a low forceps operation. Three were breech deliveries without version and 7 were breech deliveries following version. One was a high forceps delivery.

For the purpose of further study, these 67 autopsied cases have been analyzed in Table IV according to the chief cause of death found by the pathologist. Included in the same table for comparison are the 50 unautopsied cases, analyzed according to the chief cause of death determined clinically. It is instructive to note that 76 babies, or 64.94 per cent, died either from prematurity or from cerebral injury.

Of the 13 cases of asphyxia, 9 were not autopsied which gives rise to two questions; whether in all 9 this diagnosis was entirely correct and whether in some of these cases a cerebral injury may not have been associated with the asphyxia. In 3 of the 13, the baby died of suffocation while at breast; 1 of these was autopsied and 2 were not. As 5 out of the 6 cases of atelectasis were autopsied, it must be assumed that the figures for this condition are accurate.

TABLE IV

CAUSE OF DEATH	AUTOPSIED CASES	UNAUTOPSIED CASES	TOTAL
Prematurity	21	21	42
Cerebral injury	25	9	34
Asphyxia	4	9	13
Atelectasis	5	1	6
Bronchopneumonia	2	4	6
Congenital anomalies	5	2	7
Hemophilia	0	2	2
Impetigo	0	2	2
Lobar pneumonia	1	0	1
Icterus neonatorum	1	0	1
Spontaneous perforation of the intestine	1	0	1
Edema of brain	1	0	1
Hemorrhage in suprarenals	1	0	1
	67	50	117

The 7 congenital anomalies were all major defects: namely, extensive diaphragmatic hernia, spina bifida, malformation of heart, malformation of both kidneys, kink of intestines causing obstruction. The deaths of these babies as well as the 42 who died primarily from prematurity may with reason be classed as unavoidable deaths. If this is done, there remain 68 deaths for more extended analysis. These have been divided into two groups: the first, a medical group in which some condition arising postpartum was responsible; the second, an

obstetric group including those patients in whom the labor and the delivery were wholly or partially responsible for the deaths. In the first group are 22 cases, while in the second group there are 46. This is shown in Table V.

TABLE V

CAUSE OF DEATH	MEDICAL GROUP	OBSTETRIC GROUP
Cerebral injury	--	34
Asphyxia	3	10
Atelectasis	6	--
Bronchopneumonia	6	--
Hemophilia	2	--
Impetigo	2	--
Lobar pneumonia	1	--
Icterus neonatorum	1	--
Spontaneous perforation of intestine	1	--
Edema of brain	--	1
Hemorrhage in suprarenals	--	1
	22	46

In the medical group the 3 cases of asphyxia were caused by suffocation while nursing. In 2 of these cases it seemed purely accidental. In the third the question of intent arose and the case was made one for the coroner. On the ward service, even with the most careful nurse supervision, it is impossible to have a nurse with each patient throughout the entire nursing period and such accidents as these may from time to time occur.

Five of the 6 cases of atelectasis were autopsied and the diagnosis confirmed. Three of these were premature and 3 at full term. Seven babies died of pneumonia. Six had bronchopneumonia and one had lobar pneumonia. In 2 cases it was quite possibly contracted from the mothers, each of whom had an upper respiratory infection at the time of admission. Neither baby was allowed to nurse the mother until after the infection had apparently subsided. One baby nursed for the first time on the fourth day and the other nursed for the first time on the eighth day. During the eleven years this report covers, there have been three epidemics in the nursery due to an upper respiratory infection among the babies. Also during this time there have been two epidemics of impetigo; the deaths recorded were in the first epidemic. The origin of this infection was not discovered during either epidemic. The baby with perforation of the intestine was operated upon but did not survive the surgical procedure. The 2 deaths from hemophilia occurred early in the series, and by the present treatment with human blood serum or transfusion, we hope to prevent the occurrence of such deaths in the future.

In the obstetric group of 46 cases all the babies with the exception of the 10 who were asphyxiated died from some injury dependent upon either the labor or the delivery. In the 10 in whom asphyxia was given as the cause of death, the possibility exists that some of these

which were unautopsied may also have had a cerebral injury. In reviewing these cases it was found that 7 patients were delivered normally and did not warrant operative interference. There were 26 patients for whom operative interference was indicated; and we believe the interference elected was the one of choice for that particular patient even though a neonatal death occurred. This leaves 13 cases in which a neonatal death might possibly have been prevented. It is this group of deaths which we wish especially to emphasize.

The accompanying case reports give briefly the important items in each of these 13 cases. All these 13 patients except 2 had a normal pelvis. One of these had a simple flat pelvis and the other a high sacral promontory. Four cases were associated with a uterine inertia and these patients were permitted to continue in the second stage of labor for a long time. One patient ultimately delivered normally; a second (flat pelvis) was delivered by a moderately difficult low forceps, after a bag had been inserted and she had been given pituitrin; a third was delivered by a midforceps. The fourth patient had a bag introduced for dilatation of the cervix and after fifty-six hours was delivered by high forceps. In 3 cases there was very slow progress during the second stage and it was unusually long in spite of strong uterine contractions. Two of these patients were permitted to deliver normally and one was delivered by midforceps. There were 2 cases in which the head was arrested in a transverse position and 1 which remained a persistent occiput posterior. One of the patients with a transverse arrest failed to engage the head. She was permitted to continue in the second stage of labor for eight hours and ten minutes, with the infant's head floating, before a version was done. The second patient with a transverse arrest had a prolonged, dry labor of eighty-one hours. At the end of this time she was nearly fully dilated and there were signs of fetal distress. She was delivered by manual dilatation, manual rotation, and an easy high forceps. The patient with a persistent occiput posterior was allowed to continue with hard second stage contractions for seven and one-half hours before she was delivered by a Scanzoni rotation and easy high forceps. There was one case in which the cord prolapsed following the expulsion of a number five bag. Placenta previa occurred once in this group and the patient was bagged and later delivered by version. The remaining case, a patient with a premature baby, was delivered by forceps after a short second stage.

1. Primipara, thirty-nine weeks, normal pelvis. Prolonged second stage of labor, five and a half hours; slow advance, uterine inertia. After five hours the patient was given a small dose of pituitrin, and permitted to deliver normally. Baby weighed 5 pounds, 2 ounces. Condition at birth only fair. Died on sixth day, after many convulsive seizures and attacks of cyanosis. Autopsy: Cerebral hemorrhage.

2. Primipara, at term, normal pelvis. Prolonged second stage of labor three hours and ten minutes; very slow advancement, normal delivery. Baby weighed 8 pounds, 1 ounce. Condition at birth poor. Clinically: Signs of cerebral injury. Died in thirty-two hours. The baby also spit up a small amount of bright red blood and was considered a possible hemophiliac. It was given no treatment.

3. Multipara, at term, normal pelvis. Prolonged second stage of labor; three hours and five minutes of strong uterine contractions, associated with very slow advancement. Normal delivery. Baby weighed 8 pounds, 10 ounces. Condition at birth poor. Died on second day. Clinically: Cerebral hemorrhage.

4. Primipara, at term, normal pelvis. Prolonged second stage of hard labor, three hours. Head in low midpelvis. No advancement. Delivery: Low midforceps, when fetal heart began to fail. Cord once around the neck. Baby weighed 7 pounds, 1 ounce. Condition at birth poor. Lived one hour. No autopsy.

5. Primipara, at term, simple flat pelvis. Prolonged dry labor; uterine inertia. Bag for dilatation of cervix. Pituitrin 6 doses of 4 M. each at half-hour intervals to stimulate uterine contractions. Fully dilated with head in low midpelvis for three hours. At the end of this time there developed an hour-glass contraction of the uterus. Delivery: Moderately difficult low forceps. Baby weighed 9 pounds, 6½ ounces. Condition poor. Lived five and one-half hours. No autopsy.

6. Primipara, thirty-eight and a half weeks, normal pelvis. Prolonged first stage of labor; uterine inertia. Second stage five and one-half hours. Head in midpelvis. No advancement in spite of moderately strong uterine contractions, stimulated by ½ c.c. of pituitrin. Delivery: Easy midforceps after signs of fetal distress appeared. Baby weighed 5 pounds, 14 ounces. Condition poor. Died in six hours. No autopsy.

7. Multipara, at term, high promontory, transverse arrest. Normal first stage. Prolonged second stage of eight hours, head dipping, strong uterine contractions. Delivered by version. Difficulty with head at inlet. Baby weighed 7 pounds, 8 ounces. Condition at birth poor. Died in eighteen hours. Autopsy: Laceration of brain and cerebral hemorrhage.

8. Multipara, at term, normal pelvis. Wassermann, 3 plus. Prolonged dry labor eighty-one hours, uterine inertia. Head dipping, transverse arrest. After eighty-one hours almost fully dilated, signs of fetal distress. Dilatation completed manually, manual rotation, easy high forceps. Baby weighed 8 pounds, 3½ ounces. Condition poor. Died on sixth day. Autopsy: Congestion of all sinuses, vessels of cortex, and choroid plexus.

9. Primipara, at term, normal pelvis. Prolonged dry labor, bag for dilatation of cervix. Persistent occiput posterior. Second stage seven and one-half hours, strong uterine contractions without advancement. Failing fetal heart. Delivery: Scanzoni rotation and easy high forceps. Baby weighed 7 pounds, 6 ounces. Condition at birth poor; lived twenty-two hours. Clinically: A cerebral injury.

10. Primipara, at term, normal pelvis. Prolonged dry labor fifty-six hours, uterine inertia. Bag inserted for dilatation of cervix. After fifty-six hours patient was fully dilated, head only lightly engaged, L. O. A. position. Delivery: Difficult high forceps. Baby weighed 7 pounds, 6 ounces. Condition at birth poor; lived nine hours. Clinically: Asphyxia neonatorum.

11. Primipara, at term, normal pelvis. Prolonged first stage. Number 5 bag for dilatation of cervix. Prolapse of cord immediately following expulsion of bag. Patient delivered normally while being prepared for a version. Baby weighed 7 pounds, 14 ounces. Condition at birth poor, asphyxiated; died on third day. Autopsy: Multiple hemorrhages, large hematoma of suprarenals.

12. Multipara, at term, normal pelvis. Placenta previa covering two-thirds of the cervix. Number 3 bag inserted to control hemorrhage and to dilate the cervix. Bag expelled and cervix found to be four fingers dilated. Dilatation completed

manually, and patient delivered by version and breech extraction. Baby weighed 7 pounds, 4 ounces. Condition at birth poor. Lived one hour. Autopsy: Bilateral tear of tentorium with subsequent subdural hemorrhage. Large thymus.

13. Multipara, thirty-six weeks, normal pelvis. First stage of labor two hours and forty-five minutes. Second stage before interference only thirty minutes. At this time head on perineum and in R. O. P. position. Delivered by manual rotation and low forceps. Baby weighed 5 pounds, 7½ ounces. Condition good. Lived twenty-one hours. Autopsy: Rupture of right tentorium cerebelli with subdural hemorrhage.

In reviewing the above cases we cannot help being impressed with the fact that earlier intervention in each instance (except Cases 11, 12, and 13) was clearly indicated and would have given the baby better protection. In the first 3 cases an earlier delivery with forceps, instead of waiting for a spontaneous delivery would have been more conservative. In addition, the cause for bleeding in Case 2 should have been more carefully studied. If the baby proved to be a hemophilic, it should have been given blood subcutaneously or even transfused if its condition did not improve. Likewise, earlier forceps delivery was indicated in Cases 4, 5, and 6. Case 7 is a borderline. Her past obstetric history is poor, and suggests trouble. This delivery was her first one at the Woman's Hospital. The high promontory could not be determined except under an ether examination. It is certain that no patient should be permitted to continue eight hours in second stage, especially with hard contractions and a floating head. In Case 8, one of prolonged, dry labor, associated with a transverse position, the use of a bag might have shortened the first stage of labor and allowed the mother and baby to reach the onset of the second stage without exhaustion. It would seem that Case 9, persistent occiput posterior, should not have been allowed seven and a half hours of second stage labor without any interference. Case 11 has been placed in this group because we believe that a No. 5 bag should never be used on account of its tendency to displace an engaged head, thus increasing the chance of the cord prolapsing. After the patient with placenta previa had had a bag introduced, she was delivered by version and breech. As this occurred recently, we believe that probably a cesarean section should have been the procedure of choice. Certainly cases of placenta previa are more easily handled by laparotomy and with less risk to both mother and baby. Case 13 was one of premature labor at thirty-six weeks, the baby weighing only 5 pounds, 7½ ounces. The patient a para ii after only thirty minutes of second stage, with the caput already in sight, was delivered by a manual rotation for an R. O. P. position and a low forceps operation. It would seem that this patient might have rotated this head spontaneously with less risk to the baby.

Constant prenatal supervision gives to each mother and baby the opportunity of reaching term in the best possible condition. The

obstetrician strives to insure to each unborn child the best possible chance for survival. This chance depends upon (a) careful watching of both mother and baby throughout labor, (b) due consideration in the choice of operation where interference is indicated, and (c) the providing of every protection in the nursery after birth.

SUMMARY

This study of the neonatal deaths in 6000 consecutive ward deliveries occurring on the obstetric service of the Woman's Hospital shows:

1. There were 117 neonatal deaths, 19.5 per 1000 deliveries. These occurred among babies born to 110 mothers.

2. There were 91 of these 110 patients, or 82.72 per cent, who had attended the prenatal clinic.

3. There were 58 premature babies among the 117 and in 42 prematurity was the chief cause of death.

4. There were 55 babies among the 117 delivered normally. Of the 62 delivered abnormally there were 27 by forceps, 16 by breech, 15 by breech after version, 1 by vaginal cesarean section and 3 by abdominal cesarean section.

5. There were 86 mothers among the 110 who had normal pelvic measurements.

6. There were 67 babies autopsied, and of these 25 showed cerebral injury.

7. There were 49 babies in which death seemed unavoidable; 7 with major congenital anomalies, and 42 in which prematurity was the chief cause of death. In the remaining 68 cases, 22 died from conditions occurring postnatal in the nursery, and 46 from conditions dependent partially or entirely upon the labor or delivery.

8. Among the 22 deaths from postnatal conditions, 9 were due to communicable diseases and three to accident.

9. Among the 46 deaths from intrapartum conditions, 7 were delivered normally; in 26 there were complications requiring an operative interference; but the elected method of delivery seemed to have been the best for each individual case and 13 analyses suggest that some of these deaths might have been avoided.

10. Among the 13 possibly avoidable deaths, there were 10 in which an earlier operative interference might have been employed, 1 where a too early interference was attempted, 1 where the use of a smaller bag would seem to have been wiser, and 1 where a cesarean section rather than a version and breech would be the method of election.

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121 EAST SIXTIETH STREET.

(For discussion, see page 429.)

REPORT OF THE COMMITTEE OF THE OBSTETRICAL SOCIETY
OF PHILADELPHIA UPON THE INCIDENCE AND TREAT-
MENT OF THE TOXEMIA OF LATE PREGNANCY IN
PHILADELPHIA*

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IN THE spring of 1928 the then president of the Philadelphia Obstetrical Society appointed a committee to investigate the incidence of late pregnancy toxemia occurring in the practices of the members of the Society, and to present a report upon this complication of pregnancy in Philadelphia. The members of this committee were Drs. Stuart Lawrance, Clifford B. Lull, John C. Hirst, and Edward A. Schumann (chairman).

The committee prepared a condensed history form, notified each member that such blanks were available and requested that data upon all cases encountered be returned to the committee. It was agreed to limit the time covered by the Survey to fifteen months, from July, 1928, to October, 1929.

Responses from the members were generous and enthusiastic, most of the larger clinics presenting full reports, the smaller hospitals and individual obstetricians contributing the remainder. It is interesting to note that one of the earliest to return a case history was one of our associate members living in far distant California; Dr. Harry S. Fist of Los Angeles. One hundred and eleven case histories were received in all and an analysis of the facts disclosed in these histories forms the subject of the report.

Only the condition loosely known as the toxemia of late pregnancy was studied, i.e., nephritic and preeclamptic toxemia and eclampsia itself. In a number of the returned histories, certain facts were not recorded, so that the analysis may be said not to be complete, but enough details have been gathered to present a fairly accurate picture of this symptom complex, its symptomatology, physical findings and management, to give a fairly comprehensive picture of the condition as it occurs in this city and is handled by obstetricians and practitioners here.

1. *Seasonal Incidence.*—It is commonly stated that eclampsia and toxemia of late pregnancy occur more frequently in the spring and fall. This statement being in a measure borne out in the present series of cases. The seasonal incidence was as follows:

*Presented at a meeting of the Society on October 2, 1930.

January	6 cases	July	13 cases
February	5 cases	August	2 cases
March	0 cases	September	10 cases
April	7 cases	October	10 cases
May	12 cases	November	9 cases
June	17 cases	December	10 cases

The summer months will naturally show more cases because the time of this report extended through two summers, but this would not apply to the cases occurring in May and June or to those occurring in October and November. So that it may be said that in a general way there seems to be an increased frequency in toxemia of late pregnancy in the spring and fall. Among the severe cases and those having convulsions, the seasonal incidence was much the same. January, February and March showed none, April 4, May 1, June 3, July 1, August 1, September 3, October 2, November 1, December 3. Here the spring and the late autumn seem to provide the bulk of the serious cases.

2. *Age Incidence*.—The age in which toxemia occurs seems to have no bearing upon the condition, the greatest number of cases occurring at the age when the greatest number of women become pregnant. Thus in our series of patients the ages were as follows:

15-20 years,	15 cases
20-30 years,	47 cases
30-40 years,	36 cases
40 and over,	9 cases

It has been commonly said that these toxemias occur more frequently in unmarried women, but in the series under discussion 104 were married, 7 unmarried, so that the reverse would seem to be the case.

3. *Nativity*.—The nativity of the patients presented no conclusive evidences of a selective tendency, they being as follows:

U. S. A.	69	Jewish	5	
Italy	11	Irish	5,	Other foreign born, 10

4. *Parity*.—Of 105 cases in which the parity was recorded, 54 were primiparae and 51 were multiparae. These figures would indicate that primiparae are more frequently affected, inasmuch as obviously there are many more multiparae than primiparae.

5. *Prenatal Care*.—Eighty-five had had prenatal care, 23 had had none, three were not recorded. Of these patients having prenatal care, most were admitted to hospital early upon the development of the toxemia, and treatment instituted before the disease was well under way. Of the five fatal cases, two had had prenatal care, three had had none.

6. *Previous History*.—Fifteen patients reported measles in childhood, 12 scarlet fever. Ten patients gave a history of nephritis being

present before pregnancy. Of the 51 multiparae, 11 reported a definite history of toxemia of pregnancy occurring in previous pregnancies, one woman having had severe toxemia with all 6 of her children, four of whom were living. Eleven per cent, then, of all cases gave a history of pregnancy nephritis and 20 per cent of the multiparous women had suffered toxemia with one or more previous pregnancies. In this series, therefore, it may be said that eclampsia tends to recur and also tends to follow a previous nephritis.

7. *Convulsions*.—Convulsions occurred in 28 patients:

1 in 5 patients	5 in 3 patients
2 in 5 patients	6 to 9 in 4 patients
3 in 4 patients	20 in 1 patient
4 in 2 patients	Not stated in 4 patients

The nature of the convulsions is not reported, but they occurred at term in 14 women, at eight months in 7, earlier in 4, and there were 2 cases of true puerperal eclampsia. All of the women who died had convulsions.

8. *Mortality*.—Of 111 cases, 6 patients died, a gross mortality of 5.4 per cent. It must be realized that many of these patients were not seriously ill, being admitted to hospital immediately upon the onset of the toxemia, so that one must not be too greatly encouraged by the apparently low death rate. Of the 28 women who suffered from convulsions or coma, 6 died, or 21.5 per cent, but among these were three patients admitted to hospital in coma and dying less than eight hours after admission. It would seem that these cases should properly be classified as too late for treatment and that the corrected mortality should be 3 deaths in 25 patients or 12 per cent. Of the six women who died, all of the babies died, three being undelivered.

9. *Classification of Cases and History of Present Illness*:

14 cases were classified as mild
64 cases were classified as severe
28 cases were classified as eclampsia

The symptoms were those usually ascribed to the toxemia of late pregnancy, headache, generally described as severe, being present in the great majority. Nausea and vomiting were common, sharp increase of weight was noted in many charts and blurred vision, indigestion, epigastric pain, and edema completed the syndrome.

The physical examination of the patient upon admission was not well recorded on most of the histories. No thyroid alterations were remarked, 48 women were classified as having general edema and 10 slight edema. Jaundice was uncommon, it being noted in but one patient and as slight in this single instance. Heart and Pulse Rate: The pulse rate is very significant as a prognostic index as shown in

our series of cases. In 59 the rate was below 90, 20 the rate was between 90 and 110, 19 the rate was 120 and over. All of the patients with pulse rates over 120 were severely ill, the fatal cases coming into this group. Five women were noted as having heart murmurs, none of these being in the fatal group. The pulse rate in eclampsia is a most important prognostic indicator, pulse rates of 100 and over being usually associated with the more grave manifestations of the disease. Four patients had edema of the lungs, two of these died. In five patients moist râles were described, but of all those women recorded, the eye grounds were affected in 14, retinitis being present in 7 and hemorrhage and edema in 7. Pyelitis was present in 3 patients.

10. *Blood Pressure Findings.*—One hundred and seven of the 111 reports present enough data to warrant recording. For the purpose of comparison and discussion the 107 cases have been arranged according to their apparent severity into 3 stages, mild, severe, and eclamptic. The cases in each stage have been subdivided, when possible, into 3 groups, i.e., those in which:

- a) Symptoms or physical signs appeared, after a rise in blood pressure.
- b) Symptoms or physical signs appeared, before a rise in blood pressure.
- c) Symptoms or physical signs appeared, but there was no rise in blood pressure.

It is proposed to first discuss those determinations which were the most frequently and the most correctly reported.

Increase in blood pressure was the most common feature noted in the clinical histories of this series. The systolic pressure was above 200 mm. in 23 cases, between 180 and 200 in 28 patients, 150 and 180 in 43, and 120 or below in but 4. Among those women who vouchsafed a history of previous nephritis, the blood pressure was universally high, all of them being above 200 mm. systolic.

There was a rise in blood pressure in all of the 14 mild cases; but in 8 of these the rise appeared after or with the appearance of symptoms or physical signs and only 6 times before them. There was a rise in blood pressure in 57 of the 64 severe cases; but in 45 of these the rise appeared after or with the advent of signs or symptoms, and only 12 times before. In 7 there was no rise among the 64 cases. There was a rise of blood pressure in 27 of the 28 reported eclampsias, and apparently no rise in two of them. It may be deduced from this analysis that exclusive dependence on a rise in blood pressure to give one the first warning of toxemia, is not wise. It appears to fail to do so in over one-half of the mild, three-fourths of the severe, and while the data reported concerning the eclampsias are not sufficient to warrant a statement of fact, yet it would seem to be true for this stage also.

The values of the pulse pressure were lower in the mild than in the severe or eclamptic stages.

11. *Kidney*.—Albuminuria of course was the common finding. Eight patients had no albumin, 15 a trace or faint trace, while in the remaining 88 the records show heavy clouds. Tube casts were found in varying amount in 96, while 15 urines were negative for them. The casts were mainly granular, many hyaline and few blood casts.

The determinations related to renal chemistry, pathology, function, and bacteriology were more adequately reported than any other determinations except those of blood pressure.

Relation of Fluid Intake to Output.—Output was less than half of the intake: in 1 of 2 reported mild stage determinations; in 8 of 16 severe stage reported determinations; in 4 of 14 reported eclamptic determinations. Nevertheless, the output was over one-half the intake in a surprisingly large number of cases. Five cases were reported without any determination. In the reported cases both the incidence and the amount of albumin and casts increase from the mild to the severe stage. Of the 102 reported for albumin, 6 were negative. There was a lack of reports concerning glucosuria, acetone, diacetic acid, urobilin and indican, which is probably due to the dependence evidently placed on blood pressure rise to give a first warning.

Renal Function.—In summary the results may be put as follows:

In the first hour less than 38 per cent was excreted in:

3 of 4 mild stage cases reported

26 of 36 severe stage cases reported

4 of 6 eclamptic cases

In the second hour less than 22 per cent was excreted in:

0 of 4 mild stage cases reported

17 of 36 severe stage cases reported

2 of 6 eclamptic stage cases reported

Renal Bacteriology.—In the whole series but 32 determinations were made; of which 23 were negative, 6 reported *B. coli*, 2 the *B. pyocyaneus*, and 1 the *Staphylococcus aureus*.

12. *Blood Chemistry*.—The investigation of metabolism as expressed in terms of blood chemistry was not only woefully neglected but carelessly reported. Certain observations should accompany every blood chemistry value reported; otherwise the value will seldom be of either practical or theoretic worth. The observations required are:

1. Method of analysis.
2. Date of taking blood.
3. Time of taking blood.
4. Relation of the given date and time to (a) food intake, (b) glucose intake, (c) medication, (d) fluid intake, (e) convulsion, and (f) sleep.

In only 4 of the reported determinations was any effort made to supply any of this information. As most of these observations are necessary to establish the true meaning of most of the determinations, and

as the problems of carbohydrate, proteid and probably of fat metabolism are of the crucial questions of toxemia, it is earnestly urged that all Chiefs of Service:

1. Employ this method for diagnosis and prognosis regularly and consistently.
2. Lay down rules concerning the observations to be noted at the moment each specimen of blood is taken and that the specimen be so identified with these observations that the subsequent readings can be properly interpreted. A chart such as Titus has devised for blood-sugar interpretation can be easily prepared carried out or adapted to other blood chemistry readings.

Blood Sugar.—For all practical purposes the determinations reported are without value except in 3 cases. Taking the values as they stand, without knowledge of methods of analysis, time or relation, it may be cautiously said that a hyperglycemia is apparently more frequently reported than a hypoglycemia. It is obvious that such a statement is not decisive and no decisive statement can be drawn from the figures as given. However, if the various services will unite in a more standardized method of employing blood-sugar determinations, as well in the clinic as in the house, and if the readings are correlated with the required observations, much information of value would accumulate and a great deal of help in diagnosis and prognosis would be afforded the clinics. *Nonprotein nitrogen* was reported seldom except in eclampsia. As these stand, 12 of the 14 were between 30 and 40. *Urea.* As these estimations stand, of the 27 made in eclampsia, 24 were between 16 and 30. *Creatinine* was reported more generally throughout the 3 stages. The values as they stand show a steady increase from the mild to the eclamptic stage. In the mild stage none of the readings are above 1.5. In the severe stage 5 in 17 were above 2.0. In the eclamptic stage 5 in 18 were above 2.0. One in the severe and 4 in eclampsia were between 3.5 and 5.2. *Uric Acid.* Ten reports only.

CO ₂	40-50	51-60
Mild stage	3 of 3 reported	0 of 3 reported
Severe stage	8 of 13 reported	5 of 13 reported
Eclamptic	3 of 6 reported	3 of 6 reported

Van den Burgh Test.—There were reported 22 severe and 10 eclamptic determinations, of which 2 were positive, 2 gave immediate direct reaction, and 2 delayed indirect reaction. Wassermann plus 4 once in the whole series, all but 43 reporting.

Blood Counts.—Very few references to date and time, but a large number of reports, which making allowance for the increase of red cells said to be associated with pregnancy and for the increase of white cells in late pregnancy and early puerperium, seem to indicate that there is a moderate anemia in toxemia and a slight increase in the usual leucocytosis.

13. *Duration of Pregnancy.*—The earliest noted appearance of toxemia was in one patient at the fourth month, this woman had 6 living children, one termination of pregnancy with twins for high blood pressure, disturbances of vision, etc. She was admitted during the fourth month with a blood pressure of 242/140 and continual headache. She was treated by elimination, followed by hysterectomy under local anesthesia, leaving the hospital in good condition. In 6 patients the symptoms of toxemia appeared at the sixth month, in 60 at term and the remainder being scattered through the last two months of pregnancy. Only two cases are recorded of true puerperal eclampsia. Hydramnios was noted in 6 cases, oligohydramnios in one. Two patients had slight bleeding during pregnancy but in the entire 111 there was but one case of abruptio placenta, a somewhat significant fact.

Position and Presentation.—In the entire series there were but three breech presentations, the remainder being vertex and there were two pair of twins. Fetal heart sounds were noted as being present in 41, absent in 14, not recorded in 26.

Treatment.—A survey of the treatment afforded the women in our series of cases disclosed a striking unanimity of opinion among Philadelphia obstetricians as to the management of the toxemias of late pregnancy. In the mild cases elimination by means of colonic irrigation with large quantities of water, sweat baths, with purgation by magnesium sulphate. In the more severe cases the elimination treatment was continued with the addition of morphine with or without chloral, many of the reports using the term: "Stroganoff" or "modified Stroganoff." The intravenous use of glucose in 25 per cent solution was very general, a majority of the patients receiving this. A much smaller number were treated with magnesium sulphate intravenously in addition to sedation and elimination. Fifteen patients were treated with heparmone, but as the series has previously been reported by Dr. J. C. Hirst, the details will not be further considered in this survey. Venesection was employed in 7 patients, their systolic blood pressure being respectively 180, 180, 170, 176, 168, 220, 200 mm. The employment of inhalation anesthesia for the control of convulsions is not reported in a single case.

After elimination and sedative treatment had been employed for various lengths of time, most of the obstetricians induced labor either by medical means (few) or by bougies and followed this in many instances for forceps extraction or version. There were no instances of accouchement forcé. Twenty patients were delivered by forceps, 3 by version. Three women died undelivered.

There were 67 spontaneous deliveries. There were 11 cesarean sections, 9 classical, 2 cervical, the indication being fibroma uteri 1, increasing toxemia without effacement of cervix 7, contracted pelvis 2,

abruptio placenta 1. None of the mothers died, 3 infants were still-born, 1 died shortly after birth, a cesarean mortality of 0 mothers and 40 per cent babies.

End-Result.—It has been stated that 6 mothers died, a mortality of 5.4 per cent of the remaining 105, 25 are noted as showing albumin in the urine after discharge from the hospital, while 10 retained systolic blood pressure of 130 or over upon delivery.

Sixty-seven babies were alive and well, 31 were dead, and the fate of 13 is not recorded, some of them being undelivered when the patient left the hospital, not yet at term. The fetal mortality being 31.6 per cent.

CONCLUSIONS

In the year 1928, 49 women, and in 1929, 36 women in Philadelphia died of the various toxemias of pregnancy as listed under International Causes of Death, 148. This survey lists 6 deaths in 29 eclampsias alone, 14 of whom received prenatal care. Considering these facts, and likewise that the cause of toxemia is unknown, and finally considering the state of the data of laboratory investigations just summarized, it may be suspected that the prenatal clinics are not functioning as efficiently as they should. It is recommended that:

1. The Chiefs of Obstetric Services exercise definite supervision and that they attend personally and frequently the prenatal clinics of their departments, so that:
 - a. The clinics will profit by their knowledge and be inspired by their interest.
 - b. Inefficient officers and nurses may be recognized early.
 - c. The necessary routine will not degenerate into a mechanical and routine performance.
2. Exclusive dependence on a rise in blood pressure to indicate the first evidence of toxemia be avoided.
3. That more regular and more intelligent use of blood chemistry and other metabolic determinations as well as more complete uranalyses be employed in the clinic.
4. History of preexisting nephritis, or toxemia in previous pregnancies should place the medical attendant upon his guard, since all cases in this series, presenting such histories, developed severe toxemia.
5. Treatment of late pregnancy toxemia has become fairly standardized in Philadelphia, the general rule being elimination, followed by a modified Stroganoff procedure should evidence of nervous irritability develop, and further followed by induction of labor and surgical delivery in the event of failure on the part of the patient to improve. Inhalation anesthesia to combat convulsions is no longer recognized as a part of the therapeutics of eclampsia. The use of glucose is routine in many clinics. In 11 patients subjected to cesarean section, there was no maternal mortality, an excellent record.

6. The total mortality of 5.4 per cent is well on the low side in the management of this complication of pregnancy. A mortality of 21.5 per cent of all women having convulsions or coma and a corrected mortality of 12 per cent of patients coming under observation only when moribund be excluded, is well within the limits of good treatment. The fetal mortality remains enormous, 31.6 per cent. In the light of our present knowledge this death rate cannot be greatly reduced and it would seem that the efforts of obstetricians should be directed toward means of preserving more of these infant lives.

7. Patients recovering from preeclamptic and eclamptic toxemia, in general were discharged in good condition with but slight evidences of permanent kidney or cardiovascular damage. True, nephritis toxemia left the patient with permanently damaged kidneys.

Finally the committee begs to thank the members of the Philadelphia Obstetrical Society for their support and interest in this survey and to suggest that with further experience in conducting such studies, both on the part of future committees of investigation and of the contributors of case reports, much valuable data may be secured upon other obstetric as well as gynecologic problems by this new plan of study.

(For discussion, see page 439.)

Cullen, Thomas S.: *The Training of the Gynecologist.* Brit. M. J. 2: 941, 1929.

Every gynecologist should have a fundamental knowledge of medicine; he should be an abdominal surgeon and have a thorough grounding in general pathology as well as in the pathology of the particular branch which is to become his life work.

The method of training gynecologists at Johns Hopkins Hospital is as follows: Every year five of the graduating class are assigned to the gynecologic department. These men take histories, assist at operations, and work in the gynecologic and cystoscopic dispensaries. At the end of the year four of the men drop out, the fifth remaining with the department. The man thus promoted spends his second year in the study of general pathology. The third year he again returns to his specialty. He now describes all gynecologic material, supervises the cutting and staining of sections, and gives a detailed description of the histologic findings. He is also expected to work on special gynecologic problems. In his fourth year he is first assistant at operations, has general supervision of the wards and when the resident is away is in charge. In his final and fifth year he has full charge of the department, and in addition to assisting the visiting surgeons he performs many major and minor operations himself.

G. E. HUDSON.

THE TEACHING OF OBSTETRICS AND MATERNAL MORTALITY*

BY PALMER FINDLEY, M.D., OMAHA, NEB.

WE HAVE reached the first milestone of a new organization, an organization devoted to the interest of obstetrics and gynecology.

We who have been concerned with the inception of this Association of Obstetricians and Gynecologists of the Central States were heartened beyond measure by the response to our call to a preliminary meeting in St. Louis a year ago. More than 200 responded. The program presented by the St. Louis group was of the highest excellence and the demand for a permanent organization was spontaneous and enthusiastic.

I count it a rare privilege and a signal honor to be your first presiding officer and if this organization is to continue to function as it gives promise of doing, the group of men who constituted themselves as the committee on organization will have made a real and enduring contribution to the advancement of American Obstetrics and Gynecology.

It was truly an unselfish move on the part of these men, for they all personally felt surfeited with society affiliations. It was solely in the interest of our specialty and of men in the Central States who are earnestly endeavoring to perfect themselves in the art and science of obstetrics and gynecology that this Association was conceived. If obstetrics and gynecology are to keep step with the advance of medicine and surgery there must be opportunity for inspiration and self-expression among the men who are devoting their lives to the specialty. Here in the midwest such opportunities have been lacking. Local, district, and state medical societies have failed to give any considerable recognition to obstetrics and gynecology; our medical periodicals are limited in their scope and hence these men find it difficult to obtain space for their contributions. All this tends inevitably to retardation in development. It is to be hoped that this organization will supply a medium for self-expression and a source of inspiration for every man who is earnestly endeavoring to perfect himself in the science and practice of obstetrics and gynecology. Those who constitute the charter membership of this group were selected because of their position of leadership in their respective localities—they are men who will be enriched by such contacts and will in turn reflect benefit upon the communities in which they live.

*Presidential address presented at the Annual Meeting of The Central Association of Obstetricians and Gynecologists at Excelsior Springs, Mo., October 10, 1930.
A portion of this address is necessarily deleted for lack of space.

This association has wisely associated gynecology with obstetrics. Throughout the Continent and to the north and south of us the two are almost uniformly combined in teaching institutions and in practice. Here in the United States we find fully 80 per cent of all Deans of Medical Schools favor the combined chairs. Gynecology cannot and should not stand alone. Obstetric problems are not solved until the mother is restored to a perfect physical state, no matter what the time limit may be. There can be no line of demarcation between an obstetric and a gynecologic service—it is folly to make such a distinction. More than half of gynecology is the by-product of poor obstetrics, it represents in large part the morbidity of obstetrics and to a very large degree is chargeable to lack of proper prenatal and post-natal supervision.

In the Bulletin of the American Medical Association, June, 1930, we have the report of the Council on the resolution adopted at the Portland meeting requesting an investigation of the teaching of obstetrics in the United States and further requesting that "the Council make such recommendations for increasing the clinical teaching hours as might be warranted by the results of its investigations." In the report of the Council we are advised that the teaching of obstetrics has been tremendously improved since 1905—this opinion being based upon the following data:

1. Announcements of medical schools show that all medical schools offering four years of instruction have regular staffs for the teaching of obstetrics.
2. The time devoted to the teaching of obstetrics on the average compares favorably with the time devoted to the teaching of surgery.
3. In the "model curriculum," formulated in 1909 by the Committee of One Hundred, acting under the auspices of the Council on Medical Education, 650 hours was assigned to obstetrics as compared with 680 hours for surgery.
4. In the several complete tours of inspection of all medical schools, their rating in class A, B, or C depended, among other things, on the provision made by each school for instruction in obstetrics by means of (a) lectures or recitations, (b) the examination of patients in prenatal clinics, (c) the witnessing of the delivery of patients in demonstration clinics, and (d) the provision of opportunities of students to deliver maternity patients personally under supervision.
5. Not only have the Council's requirements been well met in the medical schools, but increasing numbers of maternity patients have become available whereby the recent graduates have been enabled to care personally for larger numbers of patients.
6. Even with the great improvements secured since 1900, efforts for further improvement have not been relaxed. In the Council's recent conference, for example, a special symposium on the teaching of obstetrics was arranged, in furtherance of Dr. Bloss's resolution.

From my personal correspondence with the heads of a number of obstetric departments, I am privileged to quote their comments on the above resolutions:

Dr. Jennings Litzenberg of the University of Minnesota responds as follows: "1. Of course all medical schools, offering four years of instruction, have a regular staff for teaching obstetrics, but the question is, how well trained are these staffs? Are they composed of men who have taken an extensive training in obstetrics, and how much time do they give to teaching? Also, how much of the staff is full time?

"2. I am doubtful if the second statement is correct. I am of the impression that if the investigation of the actual teaching of obstetrics would be carried on in the same manner as you did in other countries, some glaring discrepancies might be found between the teaching of surgery and obstetrics.

"3. If 650 hours are devoted to the teaching of obstetrics as compared to 680 hours for surgery, according to the curriculum, this would be quite satisfactory. The question is, would an investigation, such as I have suggested above, substantiate these hours? (I do not believe there is a school in the country that is devoting 650 hours to teaching obstetrics.)

"4. Did the committee, in this investigation of all medical schools, investigate the clinical teaching and the amount of clinical material available for such teaching? Was the teaching usually lectures and recitations, or were there large numbers of women to permit proper clinical teaching and for the students to deliver under proper supervision?

"5. I doubt that an investigation as thorough as the one you made, would substantiate the fifth statement that the council's requirements were being well met by the medical schools and that the recent graduates have been able to care for a large number of patients.

"6. The council's recent conference, in the symposium on the teaching of obstetrics, revealed that every speaker felt that the material and time for clinical teaching of obstetrics was entirely inadequate.

"Personally, I am convinced that in all probability the number of so-called didactic hours given to obstetrics are quite adequate in most schools. There are in nearly all schools at least enough hours given for lectures, recitations, etc., but I doubt if the material available, for the teaching of students in clinical hours, is adequate. The report to me sounds entirely unconvincing and from my small knowledge of the teaching of some schools throughout the country, I do not feel that the subject of obstetrics is adequately taught clinically."

Dr. Fred L. Adair of the University of Chicago observes that:

"With reference to number 1, it is undoubtedly accurate that all medical schools offering a four-year course have a regular staff for the teaching of obstetrics.

"I am skeptical about the accuracy of number 2, and doubt very much if the time devoted to the teaching of obstetrics compares favorably to the time devoted to the teaching of general surgery.

"With reference to number 3, I believe we could find no basis for objection to the assignment of practically an equal number of hours to obstetrics and surgery, but my impression is that most schools are not living up to this 'model curriculum.'

"In regard to number 4, I believe the four criteria for rating schools, so far as obstetric instruction is concerned, are all good. I believe, however, there should be added to these, (e) manikin course, and (f) postnatal clinics.

"With reference to number 5, I think it is undoubtedly correct that medical schools have made improvement in their obstetric teaching and that the number of maternity patients available for observation is increasing. The provision is, however, still inadequate for the adequate preparation of the students for the practice of obstetrics.

"Number 6 is very commendable, and I am pleased to know that a great deal of attention is being given by the Council on Medical Education to the teaching

of obstetrics. There is no doubt that the teaching of obstetrics has greatly improved in the last twenty years.

"It is probably true that much of the obstetrics which students see is either pathologic or operative. What the students really need for ordinary practice is ability to conduct the usual obstetric cases and to recognize pathologic conditions rather than an opportunity to observe and learn major obstetric procedures, which should in so far as possible be reserved for institutions and placed in the hands of especially trained men."

Rudolph Holmes, of Northwestern University, expresses the conviction that "the didactic teaching may be ever so strong, but the contact with patients in a truly organized pre- and postnatal clinic and maternity are lacking in almost every center. As a result most men graduate with a very scant knowledge of clinical obstetrics." Holmes is of the impression that "obstetrics is not taught as comprehensively as are medicine and surgery" and expresses the hope that the White House Conference will aid in solving the problem. "In the meanwhile," he adds, "there is something wrong in our teaching of obstetrics."

Dr. Frank Lynch of the University of California writes that "Since the Council of Medical Colleges has clearly shown that they have not yet accepted our problem, I feel the matter is up to the state boards. Thus far every state board in the country has kept step with the medical schools, modifying their licensing examinations so that they may correspond to the courses given in medical colleges, yet they do not realize that when one is licensed by a state examining body, they are turned loose to do anything that they feel like attempting in their practice. For many years I have felt that the public will not be properly protected until a practitioner is licensed to practice in definitely specified subdivisions in medicine. Thus one might take an examination which would license him to practice as a general medical man without doing surgery or obstetrics without showing any more evidence of apprentice training than would be obtained in his degree from the medical school. On the contrary, I believe that no state board should confer the right to practice obstetrics or surgery to anyone who has not had a proper apprenticeship. In obstetrics, I believe this means an apprenticeship which would give the student an opportunity of attending a minimum of 100 women in confinement together with proper prenatal and postnatal care.

"This conclusion has been forced on me since in a review of our work we find that our incidence of midforceps or high forceps is one to 34 cases, that is, if the student is to see anything more than low forceps or breech extractions, he must plan for at least 50 cases. There is no doubt whatsoever but that a student who has seen only low forceps and who attempts the extraction of an occiput posterior in transverse arrest and fails, the next time will turn to cesarean section which, unless he has had an apprentice training, he should not undertake. There is nothing new in this observation nor in our thought that an apprentice training is necessary. The fact that it has safeguarded the public in the countries in which it is attempted is well evidenced by the obstetric situation in the Scandinavian countries."

Dr. A. M. Mendenhall of the University of Indiana gives the encouraging report that the department of obstetrics in Indiana has been given practically double time for teaching. "I am," he writes, "much enthused over the bloc system which I have adopted here and a copy of which I sent you a few weeks ago. Every twelve students have six weeks during which time the whole time is given to obstetrics. We have gotten this into the curriculum in addition to the regular lectures, recitations, quizzes and clinics. This is a step forward, but we need a few more steps. More time should be allotted to obstetrics than to surgery. A beginner in practice does much more obstetrics than he does surgery. He should be thoroughly taught those things which he is most likely to be called upon to do,

and which can be easily shown to be general medicine, obstetrics and a small amount of minor surgery. I agree with this but would add that a very careful supervision home delivery service by a student is advantageous but if he is merely allowed to act as a stork and is not followed up by competent teaching, it is poor obstetric pedagogy."

The only criticism offered by Dr. Barton Hirst of the University of Pennsylvania is with reference to the use of hours assigned to instruction in obstetrics. He much prefers the European system of blocks of time.

Dr. Joseph DeLee of the University of Chicago is of the opinion that "while theoretical instruction may be enough—practical work on patients and research are both as yet deficient."

Dr. Percy W. Toombs of the University of Tennessee writes: "I am importuned daily to teach my students operative obstetrics. I believe students should be taught normal obstetrics during their collegiate course and given only the most essential of emergencies in obstetric practice. I believe operative obstetrics should be given in a postgraduate course just as the refined technic of the various specialties in general surgery are now given.

"Does the general practitioner of medicine enter the special field of eye, ear, nose and throat or that of specialized abdominal surgery without special preparation? If he does not why should he be allowed the privilege of bartering human life at its very beginning without preparation?

"Until provision is made in the curricula of medical schools for such preparation the present distressing high rate of mortality will continue. If there is to be any reduction in maternal mortality there must be a more widespread knowledge and clearer understanding of the importance of the principles underlying proper obstetric care.

"With proper supervision of the pregnant woman the lives of many mothers would be saved who are otherwise sacrificed upon the altar of maternity."

Dr. L. A. Calkins of the University of Kansas writes: "It seems to me that the statement of the Council in the Bulletin of June, 1930, is quite inadequate and does not give the matter anything like its due consideration. Inasmuch as the obstetrics of the future is going to be more and more in hospitals, it seems to me that medical students should have considerable more obstetric training as it is done in hospital practice. It is very much easier to provide adequate instruction from the hospital cases than it is for outside deliveries. We are also badly in need of opportunities for postgraduate instruction in this country."

Dr. E. D. Plass of the University of Iowa finds the report of the Council so general that he fails to see any value in it. To provide more adequate clinical facilities Plass would have our schools affiliated with maternity hospitals—to do this "artificial barriers must be broken down or extended." With less than a delivery a day, Plass finds that he is lacking in clinical material for the instruction of his students.

"I agree with you," writes Dr. Jeff Miller of Tulane University, "that in spite of the improvement, there should be no relaxation in the efforts of the various organizations to continue the improvement, for there is still room for it. Any specialist who sees complicated and badly managed cases knows that, and any man who has had, as I had for many years, a service in a public hospital devoted to that sort of case, wonders if things are really any better. A ward of that variety gives much food for thought. Certainly there is no subject in which the young physician so much needs training, for he still gets a large part of his practice in the first years from maternity cases, and he is still too much inclined to treat them as all in the day's work rather than as conditions which need his best efforts and which may in a moment develop complications of the utmost gravity. On the other hand, I think we should emphasize without ceasing the fact

that the majority of labors are not pathologic but physiologic, and that it is the first task of the physician to keep them normal."

Dr. Franklin S. Newell of Harvard University writes as follows:

"The copy of the report of the Council of the A. M. A. on the teaching of obstetrics seems to me to say very little. My own impression is that since obstetrics came to be considered a specialty, even though it is recognized as one of the fundamental clinical subjects, more and more time is devoted to surgery and less and less to the teaching of obstetrics. I will admit that we have much more chance for clinical teaching than we used to. We have in the third year ten days to two weeks devoted to district work where the men do nothing else, and we have four weeks in the fourth year where the men give their full time to obstetrics. On the other hand, we have only thirty-six hours for lectures and demonstrations where we had ninety-six hours when I was a student. I do not believe that the theory of normal obstetrics and the complications can be properly demonstrated to a class in thirty-six hours, and I think that the theory should be driven home very thoroughly in the second and third years so that the men can appreciate their clinical work.

"All of our clinical departments have had their didactic teaching hours cut in the last two years so that more time could be devoted to clinical work in the hospital. All of these hours which have been saved by cutting down the number of lectures, demonstrations and recitations have been added to the clinical teaching of medicine and surgery, and none of it has gone to obstetrics. Perhaps we have been better organized than the other departments or at least organized at an earlier date and we may not need the increase in time as much as they do, but in the last few years we have been definitely cut for the benefit of the other departments."

Dr. Sproat Heaney of Rush Medical College, Chicago, expresses surprise at the report of the Council on Medical Education and says:

"I have no doubt at all that obstetrics is well taught didactically in all medical schools. The great difficulty in America, however, is the deficiency in clinical teaching and the paucity of clinical beds for obstetrics. Internal medicine and surgery almost everywhere have sufficient beds for the thorough teaching of clinical medicine and clinical surgery. Hardly anywhere are there enough beds to teach obstetrics as it should be taught. The clinical teaching of obstetrics is relegated to the Out-Patient Department and when objection is made to this the non-obstetricians say, 'Obstetrics should be taught in the home because most mothers are delivered in their homes.' Delivery in the home is not objectionable except that the teaching is done by the externe while the professor of obstetrics and the well-trained instructors in consequence have little to do with the clinical teaching of their branch. Why should surgery and medicine be properly taught by experts while the clinical teaching of obstetrics is delivered over to the most ignorant members of the obstetric staff?

"Furthermore, obstetrics should have more than its normal 'proportion of clinical beds.' Every medical case and every surgical case is per se pathologic and abnormal while the obstetric cases are mostly normal and it requires so many cases before the student meets an abnormal case."

Dr. John Polak of the Long Island College and Hospital expresses dissatisfaction with the report of the Council in that it has failed to meet the issue squarely. He is of the impression that in 60 of the 78 medical schools in the United States, prenatal clinics are lacking or of doubtful character and adds: "There is no question that there is and has been great improvement in the teaching of obstetrics since 1900, but the whole thing is so poorly arranged and so belittled that the students do not get the impression that obstetrics includes a knowledge of medicine, pathology, physiology, biochemistry, serology as well as surgery. If

every school would adopt the plan of instruction mapped out at the Chicago Conference the whole plane of obstetric teaching would be elevated."

Dr. Brooke Bland of Jefferson Medical College, Philadelphia, has developed within a period of five years one of the best departments of obstetrics in the country. He has the following to say:

"In Jefferson something more than 200 hours are devoted to instruction in obstetrics and gynecology. This does not include the work done in the Out-Patient Service, the time spent in witnessing ten to twenty deliveries in a Lying-In Hospital, covering a period of one week, nor witnessing deliveries in their senior year, in our Maternity. I believe that the statement made is somewhat in error. I do not believe there is any medical school in the United States that devotes 650 hours to the teaching of obstetrics and gynecology, nor do I believe it is necessary to set apart that much time for the consideration of the subject. I do not believe it possible to devote 650 hours to the study of obstetrics in a college curriculum. I cannot conceive how it would be possible to arouse interest in the student and make so long a time attractive.

"I find that all the suggestions submitted are followed in my Department at Jefferson, except the provision of opportunities for students to deliver maternity patients personally. I do not think this is a wise course. I would hesitate to adopt it in my department. I believe that more harm than good, especially for the patient, would follow the procedure. An obstetrician cannot be made in the classroom, regardless of the number of hours devoted to obstetric instruction. I would go further and say that entirely too much time is devoted to the teaching of major surgery and certainly some phases of the subject that nine students out of ten will never have occasion to practice.

"Unquestionably the facilities for teaching obstetrics have been enlarged tremendously during the past few years and I am quite convinced that the men graduating today are better prepared than any time in the history of obstetrics, in our country."

We appreciate the interest the Council has manifested in our problem, but we frankly dissent from some of their deductions. We grant that there has been much improvement in the teaching of obstetrics since 1905 but the progress made has not been commensurate with that made in the teaching of medicine and surgery in the same period of time. There is evidence on every hand that obstetrics is receiving more favorable consideration at the hands of our teaching institutions. Larger clinical facilities are being provided and more and more stress is placed on clinical instruction in obstetrics. But the teaching of obstetrics in our medical schools has lagged far behind that of surgery and medicine and even that of some of the minor subjects. Once the governing board of our teaching institutions become cognizant of the axiom that it is the business of our undergraduate medical schools to prepare their students for the general practice of medicine, there is little difficulty in bringing about a more generous consideration of the need for more and better clinical instruction in obstetrics.

It is gratifying to learn from the report of the Council that the announcements of medical schools offering four years of instruction reveal that all have regular staffs for the teaching of obstetrics. It had not occurred to us that the announcements of our schools would fail

to list a teaching faculty in obstetrics—such an omission would be needless economy in space and printer's ink.

The statement that the time devoted to the teaching of obstetrics compares favorably to the time allotted to the teaching of surgery is a finding of the Committee of the Council that is misleading. A few years ago the ratio of teaching hours in surgery as compared with obstetrics was as 4.5 is to 1. It is now about as 2 is to 1—this is progress. Furthermore, it is contended that it is not a matter of numbers of teaching hours but rather of how the teaching hours are employed. It is our contention that as compared with surgery the teaching of clinical obstetrics is woefully lacking in the major portion of our medical schools. Not less teaching of theory but more clinical teaching is the need of obstetrics.

We do not need to look to our less favored institutions alone for verification of our contention. There are schools in the United States of the highest order where clinical surgery is provided for in overabundance and where clinical obstetrics receives scant recognition. A recent visit to one of our foremost teaching institutions revealed a magnificent hospital of a thousand beds, with space and equipment for the clinical teaching of surgery that is unexcelled, while obstetrics is relegated to an antiquated outbuilding where students do not have sufficient material at their disposal to provide sufficient cases for even a portion of the student body. Here there are eight admissions to the surgical department to one to the obstetric department. Excellent didactic instruction is given by a faculty of the highest order but the lack of clinical material falls far short of the minimum requirements. And this in an institution that has four times the number of clinical beds required for teaching purposes.

I refer to this institution as a striking illustration of the inadequacy of clinical teaching in obstetrics and such examples are not exceptional. It is difficult to understand how in "the several complete tours of inspection of all medical schools" the lack of prenatal instruction and the sparsity of clinical facilities in obstetrics in most of our teaching institutions could have escaped the notice of the investigators. It is heartening to note in the report of the Council that their efforts looking to the further improvement in the teaching of obstetrics have not been relaxed. It is our cherished wish that the future efforts of the Committee on Medical Education will not be as abortive as in the instance just disclosed. I am indebted to Rudolph Holmes for the information that no obstetrician served on the committee of the Council—this I have since verified. The department of obstetrics had no friend in court, no one to plead its cause and judging from the brevity and evasiveness of the report the whole matter was none too seriously taken.

We will hope for better results in the future and we are not disheartened in contending for a square deal for obstetrics. Progress has been made and the good work will go on until obstetrics receives its just recognition.

446 AQUILA COURT.

AN ANALYSIS OF 128 INTERPOSITION OPERATIONS

BY PAUL MESHBERG, M.D., PHILADELPHIA, PA.

(From the Gynecological Service of the Mt. Sinai Hospital)

THIS paper is based upon an analysis of 128 interposition operations performed for prolapse of the uterus at the Mt. Sinai Hospital, covering a period of eight years from 1922 to 1929 inclusive.

The 128 patients upon whom interposition operations were done were taken from two gynecologic services: 46 cases from the service of the late Dr. John Cooke Hirst, and 82 cases from the service of Dr. Charles Mazer.

AGE

The youngest patient was twenty-four years old, the oldest sixty-five years. The average age of this series was forty-two and thirty-two hundredths years.

TABLE I. AGE

6 patients were between 24 and 30 years old
19 patients were between 30 and 35 years old
36 patients were between 35 and 40 years old
39 patients were between 40 and 50 years old
23 patients were between 50 and 60 years old
5 patients were between 60 and 65 years old

TABLE II. SYMPTOMS

	CASES
Sensation of prolapse	88
Urinary frequency	58
Backache	41
Pain in lower abdomen	39
Leucorrhea	29
Menorrhagia, metrorrhagia, dysmenorrhea	23
Dragging sensation in pelvis	22
Incontinence of urine	11
Sacro-iliac pain	10
Rectal complaints	4
Pruritis vulvae	3
Constipation	2

The symptoms usually complained of in this series were sensation of prolapse, urinary frequency, incontinence, backache, pain in lower abdomen, leucorrhea, dragging sensation in pelvis, dysmenorrhea,

metrorrhagia, menorrhagia. Of these symptoms, the most complained of was sensation of prolapse, the next was urinary frequency.

The symptom of constipation is recorded in this series in only two cases, while other authors report this symptom in a greater percentage of cases. It is possible it was either overlooked, or the patients did not lay stress on it.

PATHOLOGY

Among the pathologic findings there were prolapse of first, second, and third degree, cervical erosions, cervical polyps, external and internal hemorrhoids, and retroversions.

TABLE III. PATHOLOGY

	CASES
Prolapse:	
First degree	29
Second degree	73
Third degree	26
Cervical erosions	21
Cervical polyps	4
Hemorrhoids, external and internal	14
Retroversions	9
Abcessed kidney with stones	1
Uterine subserous fibroids	2
Ventral hernias	2
Diabetes	2
Orthopedic deformity	1

OPERATIONS

Watkins' interposition operation was done in 122 instances, modified Watkins' in 5 instances, Wertheim's in one.

TABLE IV. OPERATIONS

	CASES
Watkins' interposition	122
Modified Watkins'	5
Wertheim's operation	1
Amputation of cervix	92
Curettage	50
Hemorrhoidectomies	14
Perineorrhaphies	128
Ligation of tubes	37
Myomectomies by vaginal route	2
Appendectomy	1
Exploratory laparotomy	1
Correction of ventral hernia	2
Plication of vesical sphincter	2

The Watkins' interposition operation was done on patients near menopause or past that age, and the modified operation was done on patients of childbearing age and below thirty years of age, where future pregnancies were considered. The tubes in these cases were not ligated. The modification consists in placing the first suture at

the level of $\frac{1}{2}$ an inch below tubal insertion on anterior uterine wall and through vaginal fascias about $\frac{1}{3}$ distance from urethra to cervix, not bringing the uterus through the peritoneal opening made.

The Wertheim's operation was done in one instance only because it was found on doing laparotomies on a few patients after they had had a Watkins' interposition operation some time before, the anterior peritoneal flap was firmly adherent to the uterus posteriorly, just as if it had been sutured to it.

Every one of the 128 patients had a perineorrhaphy.

The tubes were ligated in all patients near the menopause and where no more pregnancies were desired. In patients past menopausal age, the tubes were left alone. In patients, where future pregnancies were desired, the tubes were not touched and a modified Watkins' interposition operation was performed.

There must be some discrepancy in the figures reported in this series, as eleven patients complained of incontinence and only 2 had plications of vesical sphincter. Undoubtedly some by mistake were not recorded. The number of amputations of the cervix here reported is also small, as practically every patient who had a prolapse, had an amputation of the cervix with the interposition operation.

As a rule, the invariable procedure in the correction of prolapse of the uterus at the Mt. Sinai Hospital in every instance is amputation of cervix, Watkins' interposition operation. Häger's perineorrhaphy, ligation of tubes if near menopause, plication of vesical sphincter if there is incontinence, and curettage if metrorrhagia, menorrhagia, or dysmenorrhea are present.

Some patients had in addition to the interposition operation, some other operation at the same time. Two patients had myomectomies through the vaginal route, one had an appendectomy, one an exploratory laparotomy, 2 had correction of ventral hernias, 14 had hemorrhoidectomies at the same time the interposition operation was done.

COMPLICATIONS

The most troublesome complication was postoperative cystitis. Others are apparently more fortunate in this respect; their percentage of cystitis is much smaller. This can be explained by the fact, that most of the patients in this series were Jewish women, highly emotional, unable to void voluntarily while lying in bed. Almost every patient, with few exceptions, had to be catheterized several times a day for a few days after the operation, and some of them every day until they were able to stand on their feet. This resulted in a great number of bladder infections. Lately we started to use an indwelling mushroom catheter; this does away with frequent catheterizations, but does not prevent bladder infections.

We lay much stress on bladder infections, no case is overlooked. A catheterized specimen of every postoperative patient having had an

interposition operation was sent to the laboratory every third day and if the report came back with over 6-8 W. B. C. per high power field from a centrifuged specimen of urine, that patient was considered having cystitis. All patients with cystitis had bladder irrigations daily with 1:4000 silver nitrate solution until they cleared up.

One patient developed an acute attack of cholecystitis while recuperating from the interposition operation and had to have a cholecystectomy. Another patient unfortunately developed a pulmonary embolism and died.

TABLE V. COMPLICATIONS

	CASES
None	46
Cystitis	71
Suture infections	5
Phlebitis	4
Pneumonia	3
Shock during anesthesia	2
Parametritis	1
Pyelitis	1
Cholecystitis	1
Pulmonary embolism and death	1

STAY IN HOSPITAL

The lowest number of days of stay in hospital was fifteen days, the highest was sixty-four days, the average number of days was twenty-two. The complications developing after the operation were responsible for the patient staying in the hospital longer than fifteen to seventeen days, which is the usual number. One patient on Dr. Mazer's service had a nephrectomy first and two weeks later had an interposition operation.

MORBIDITY

Any rise in temperature above 99° F. was considered as morbidity.

TABLE VI. MORBIDITY

	CASES
None	33
Between 99° F. and 101° F.	67
Between 99° F. and 102° F.	13
Between 99° F. and 103° F.	7
Between 99° F. and 104° F.	3
Between 99° F. and 105° F. and above	2

END-RESULTS

The end-results were obtained in the following ways:

1. Through the records of the gynecologic clinic for clinic patients.
2. By direct examination of patients in the gynecologic clinic or in the office when possible.

3. Through the office records of Dr. Charles Mazer for his private patients.

4. Through letters mailed to patients in which they were requested to come for an examination and if unable to come to answer certain questions pertaining to the result of the operation.

Of the 128 patients, 92 were traced, one died, and 35 were untraced. Of the 92 traced patients, 83 had good anatomic results, 3 fair, and 6 had failures.

The 3 patients with fair anatomic results had recurrences of rectoceles, but the prolapse was cured. Adding the 3 fair to the 83 good, there is a total of 86 patients cured anatomically or 93.5 per cent, and anatomical failures 6.5 per cent.

Symptomatically 71 patients had good results, 14 fair, and 7 had bad results. Of the 14 patients with fair symptomatic results, 11 complained of urinary frequency, 3 of urinary frequency and incontinence, one of backache and sacroiliac pains. One patient was symptomatically worse than before the operation although the anatomic result was good.

Of the total 92 cases traced, 68 had good anatomic and good symptomatic results, 3 patients had fair anatomic and good symptomatic results, 14 patients had good anatomic and fair symptomatic results, one patient had good anatomic, but poor symptomatic results, 6 patients were failures anatomically and symptomatically.

If we consider the patients with fair symptomatic results as cured, because all of them had minor complaints and the prolapse was cured, adding the 71 cases with good symptomatic results to the 14 cases with fair results, we will have a total of 85 patients cured symptomatically. This leaves 7 patients with poor symptomatic results as failures or 7.6 per cent failure symptomatically.

TRACING TIME

The length of time elapsed since the operation up to the date the patients were last seen varied from three months to eight years.

TABLE VII. TRACING TIME

40 patients traced between 3 months	to 1 year	from date of operation
11 patients traced between 1 year	to 2 years	from date of operation
7 patients traced between 2 years	to 3 years	from date of operation
7 patients traced between 3 years	to 4 years	from date of operation
9 patients traced between 4 years	to 5 years	from date of operation
5 patients traced between 5 years	to 6 years	from date of operation
9 patients traced between 6 years	to 7 years	from date of operation
4 patients traced between 7 years	to 8 years	from date of operation

The majority of women operated upon in this series belonged to the poor class, and as soon as they came home from the hospital they started to work, putting the recently performed operation to a severe test. Therefore, if in those patients who were examined three months

after the operation, good results were found, undoubtedly the operative results must be good even a few years later.

There was no difficulty in tracing all those patients reported in this series with some symptomatic or anatomic complaints, because they usually came in voluntarily for examination and expecting to be treated, feeling that the surgeon did not complete his work and owes them more treatments. Everyone with some complaint usually came in two or three weeks after being discharged. As a matter of fact every patient upon discharge was instructed to come for an examination six weeks later either to Dr. Mazer's office, or to the gynecologic clinic, or to the family physician who referred the case for an operation, and if the results were found good, they were further instructed to come back if any complaint arises. It was impossible to miss partial or complete failures.

Some difficulty was met in tracing those patients with good anatomic and symptomatic results, as some of them receiving the letter to report for an examination answered they do not see any necessity to come, because they feel all right and there is nothing wrong with them.

Of the 35 untraced patients, 20 changed their addresses and could not be located, the other 15 did not respond.

DISCUSSION

Reviewing the literature for the last ten years on correction of prolapse of the uterus and end-results of such corrections, I found that no matter what form or method of an operation a surgeon selected for the correction of prolapse of the uterus, the average failure among different surgeons, at different hospitals, was between 10 and 12 per cent. In other words, each surgeon gets practically the same results, although he does it differently than the other.

It is not the writer's intention to criticize any form of operation for prolapse of the uterus nor to praise, but to bring facts as they are and to be taken at their worth.

Some gynecologists claim that the Watkins' interposition operation is the best for prolapse of the uterus on women near or past menopause, provided the uterus is not too large nor too small, and there is no pelvic inflammation. Other surgeons condemn it and under no circumstances would perform this operation, they resort to ventrosuspensions or ventrofixations followed by a vaginal plastic. Are these men right or wrong?

I believe that they are right, because the best operation for prolapse of the uterus is the one that gives success to the individual surgeon. One form of an operation for prolapse of the uterus may be a success in the hands of one surgeon, at the same time, the same operation and the same technic may be a failure in the hands of another surgeon.

To the gynecologists of Mt. Sinai Hospital, Watkins' interposition operation is the most logical and simple operation for prolapse of the

uterus, in selected cases near or past the menopause and when the uterus is not too large or too small.

SUMMARY

1. There were 128 interposition operations performed at the Mt. Sinai Hospital on two gynecologic services from 1922 to 1929 inclusive.

2. Ninety-two patients were traced, one died, and 35 patients were untraced.

3. Of the 92 cases traced, 83 were successful anatomically, 3 cases partially successful, 6 cases were failures or 6.5 per cent failures anatomically.

4. Of the 92 patients traced, 71 cases were successful symptomatically, 14 partially successful, and 7 cases were failures, or 7.6 per cent failures symptomatically.

5. The 14 patients partially successful symptomatically complained of one or two minor symptoms but the prolapse was cured, or 15 per cent partial success symptomatically.

6. The average failure of all forms of operations for prolapse of the uterus among different surgeons was from 10 to 12 per cent.

The writer wishes to acknowledge the kindness of Dr. Charles Mazer for helping him to trace the private patients and allowing him to utilize the office records.

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A SIMPLE, RAPID PROCEDURE FOR THE LABORATORY DIAGNOSIS OF EARLY PREGNANCIES

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AN EXAMINATION of the work of Louria and Rosenzweig,¹ Brouha and Simonet,² Erhardt,⁴ and Bruhle³ could hardly fail to convince one that the test for pregnancy described by Zondek and Aschheim⁵ is of great practical value. Yet this test, admirable though it is, has some distinct disadvantages, one of which may make it impractical in a laboratory or hospital not closely affiliated with some university or institute. To perform the Zondek-Aschheim test it is essential to be in a position to command a ready supply of immature mice weighing from six to eight grams. If a large breeding colony of mice is not easily available, some difficulty might be encountered in procuring suitable animals at the time a test was desired. Moreover, even if one had at hand enough of the immature mice to answer the calculated requirements for a given week, and, for some reason or other the number of samples submitted fell below expectations, the unused animals would soon mature beyond their usefulness, so that another group of the immature animals would have to be gotten.

It is believed that the procedure to be outlined here obviates this difficulty as well as some others inherent in the Zondek-Aschheim procedure. Our method rests upon three fundamental facts:

1. The ovaries of an isolated, unmated female rabbit contain neither corpora lutea nor corpora hemorrhagica, inasmuch as the rabbit does not ovulate spontaneously, but only after coitus.
2. The urine of pregnant women contains some substance, or substances, which simulate in their biologic effects the anterior lobe of the pituitary.
3. The ovary of the rabbit quickly responds to the injection of these substances by the formation of corpora lutea or corpora hemorrhagica.

The first fact has long been known, and has been used to advantage in the study of the reproductive activities of the rabbit.⁶ The second fact, namely, that the urine of pregnant women contains the biologically active substances, was reported by Zondek and Aschheim, and is utilized by them in their test for pregnancy. That the ovary of the rabbit would respond promptly to the injection of urine from pregnant women was noted in some studies on the mechanism of ovulation in the rabbit,^{7, 8} and confirmed by Jares⁹ and by Hill and Parkes.¹⁰

TECHNIC

The materials and equipment necessary for the performance of the proposed test are: (1) an ordinary bedpan specimen of urine, (2) a five c.c. syringe, and (3) an unmated, mature female rabbit. The urine is injected intravenously thrice daily for two days in 4 c.c. doses. Forty-eight hours after the first injection the rabbit is killed. If the ovaries contain either fresh corpora lutea or large bulging corpora hemorrhagica, the reaction is positive and the patient who furnished the sample is presumably pregnant. If the ovaries contain neither corpora lutea nor corpora hemorrhagica, but only clear, unruptured follicles, regardless of their size, the reaction is negative.

A. The selection and maintenance of rabbits.—Inasmuch as the period of gestation in the rabbit is from thirty to thirty-two days, one may be certain that adult females strictly isolated from males for this period of time will not be pregnant, and that their ovaries will not contain either of the structures which characterize a positive reaction. Yet, if a number of females are kept together, it is possible that one doe may be "hopped" by another in heat and enter a period of pseudopregnancy which would last for about twenty days.⁶ It is desirable, therefore, that the females be kept isolated not only from males, but from other females as well by placing them in individual cages. It is not a difficult matter to arrange with a rabbit dealer to have a sufficient stock of females kept isolated in just such fashion for the desired period.

If by any chance, this is found difficult to arrange, one may buy adult females indiscriminately on the market and immediately place them in separate cages. After an interval of three weeks one can easily determine by palpation which of the rabbits are pregnant. Those that are found to be not pregnant at this time may be used immediately. In the event that some of the animals deliver young during this period of isolation, they may be used within twenty-four hours after parturition. Indeed, an animal that has just delivered a litter is a most desirable animal for the test.

In case, one has not had opportunity to isolate the rabbits for the desired period, and it is found necessary to perform a test, it is safe to use a rabbit that has been isolated in the laboratory for only eight or ten days. Even if the rabbit in question had had coitus just before it was obtained, the corpora lutea of pregnancy or pseudopregnancy would then be at least eight or ten days old, and could not be confused with the fresh corpora lutea or corpora hemorrhagica produced by the injections of an active urine.

Briefly, then, one may safely use all rabbits that are not demonstrably pregnant at the end of three weeks of isolation. In time of stress it will not cause confusion to inject a rabbit that has been isolated for only ten days, since the autopsy will disclose either that the corpora lutea are fresh, having been produced by the injections, or, that the injected animal was pregnant or pseudopregnant, in which case the result of the test might be discarded and another animal subjected to the injections.

It is understood, of course, that once the rabbits have been isolated for a sufficient length of time, they may be used at any time afterward.

B. The storage of the samples and the injections.—It is desirable to place the specimens on ice soon after collection. After the urine has become cooled a precipitate is likely to settle. If the urine is filtered while cold the precipitate may be removed without causing a noticeable loss of potency of the sample. Before each injection it is necessary to warm the sample in hot water for a few minutes so as to prevent shock to the animals. One must guard against overheating of the urine, however, for prolonged heating at 45° C., or more will decrease the potency of the specimen. After each injection the urine should be

returned to the cooler. No aseptic precautions are necessary either in the storage of the samples or during the process of the injections. If the material is handled in the manner just described, the potency of the active samples will not be materially impaired at the end of six days.

RESULTS

We have examined a total of 111 urine samples by our method. Of these, three proved to be so toxic that it was impossible to carry out the test. Of the remaining 108 specimens 25 were obtained from women in the last months of pregnancy, and each of these gave a positive reaction. In addition to these 25, positive reactions were obtained from the urines of 32 women presenting themselves to the maternity clinic for diagnosis at a time when a certain clinical diagnosis could not be made. We have been able to follow 22 of these 32 cases so as to check the laboratory diagnosis either by the detection of fetal heart sounds, or by unimpeachable evidence of abortion or miscarriage. An analysis of the thoroughly checked cases in which a positive reaction was obtained is presented in Table I.

TABLE I. CASES GIVING POSITIVE REACTION, SATISFACTORILY CHECKED¹

STAGE	NUMBER OF CASES	REMARKS ON SUBSEQUENT CLINICAL HISTORY
7-9 months	25	Normal pregnancies—delivered
3 months	1	Normal pregnancy—delivered
10 weeks	1	F. H. S.
6-8 weeks	1	Suspected tubal pregnancy—Laparotomy
	1	Spotted once a month during pregnancy— F. H. S.
	2	F. H. S.
4-5 weeks	2	Irregular bleeding throughout pregnancy— F. H. S.
	5	F. H. S.
	1	Pernicious vomiting—aborted
	2	Miscarriage
	1	Aborted
3 weeks	1	F. H. S.
2 weeks	1	Ectopic, ruptured, laparotomy
	2	F. H. S.
10 days	1	Pulmonary T. B.—aborted
Total	47	

¹In the column at the extreme left the stage of pregnancy at the time the sample was submitted is expressed in days, weeks or months since the first missed period. Under Subsequent Clinical History is indicated the ultimate fate of the pregnancy, "F. H. S." indicating fetal heart sounds detected, but pregnancy as yet not completed.

There remain the ten cases yielding positive reactions which we have been unable to check by the criteria we have chosen; namely, the detection of fetal heart sounds, or indisputable evidence of abortion or miscarriage. An analysis of these cases appears in Table II.

Of the 51 specimens giving negative reactions, two were obtained from normal males. Twenty-five were secured from women in the medical wards, known to have been nonpregnant at the time the test was performed. Among these cases were three of carcinoma of the ovary, two of carcinoma of the fundus uteri, one of carcinoma of the

cervix, and one of mediastinal tumor. The other specimens of this group were from convalescents in the medical ward. Twenty-four of the 51 negative reactions were gotten from the urine of women applying to the maternity clinic for diagnosis, and suspected of pregnancy at the time the sample was submitted. In 18 of these 24 women the possibility of pregnancy has since been excluded. We have lost contact with the other six.

Briefly, the laboratory diagnosis by our method has agreed with ultimate clinical diagnosis in each of the 92 cases for which we have adequate data. Although a final check has not been obtained on ten positive reactions, and on six negative reactions, we have so far been unable to discover a single error.

TABLE II. POSITIVE REACTIONS IN CASES NOT SATISFACTORILY CHECKED

STAGE	NUMBER OF CASES	REMARKS AND PRESENT CLINICAL DIAGNOSIS
3 months	1	Irregular bleeding, 4 months pregnant
7 weeks	1	Lost
4-5 weeks	2	Lost
	2	3 months pregnant
	1	History of miscarriage during third month of last pregnancy. Had profuse bleeding during third month of present suspected pregnancy. No physician present at the time to make certain of miscarriage. Ten days later specimen obtained which gave a negative reaction.
3 weeks	1	Too early for clinical diagnosis
13 days	1	2 months pregnant
11 days	1	3 months pregnant
Total	10	

DISCUSSION

From our results it seems obvious that the method we propose is adequately accurate for routine clinical use. We do not regard it as significant that the error by our method has so far been zero, while that of the Zondek-Aschheim test has been from 1 to 2 per cent. It is likely that if we had had more material, we might have encountered an error or two. There is further the possibility that in a number of rabbits kept isolated for several months the ovaries of a few may contain some follicles showing hemorrhagic degeneration. Although we doubt that the shrunken, degenerating follicles showing partial or complete hemorrhagic change will ever be confused with the large, bulging corpora hemorrhagica produced by the injections, one must recognize this source of error as possible though hardly probable. So far we have encountered this phenomenon of degenerative change but once, and in this instance the hemorrhagic follicles were shrunken to the size of pinpoints and could be confused with the corpora hemorrhagica of a positive reaction by no one.

Of course, there is also the disadvantage of toxicity in a small percentage of urines. This is quite as true of the Zondek-Aschheim procedure. With our method, we found 3 of 112 specimens too toxic to yield satisfactory results. Zondek reports that about 6 per cent¹¹ of the samples submitted were too toxic to be handled, and to obviate this difficulty, he has devised a method by which these toxic urines may be made innocuous. Since the appearance of this paper we have not encountered a sample with which to test his procedure.

Compared with the minor disadvantages of the use of the rabbit as we have proposed, are several real advantages. In the first place, the test as we have used it may be completed in forty-eight hours, as contrasted with one hundred hours for the performance of the original Zondek-Aschheim test. In an effort to decrease the time necessary for the performance of a test, Zondek proposes a method¹¹ of concentrating the active substances in the urines of pregnant women so that the test may be completed in about fifty hours. With this modified



Fig. 1.—A typical positive reaction showing the corpora hemorrhagica produced by the injections of urine from a pregnant woman.

technic, however, only positive reactions are significant. Really, if one were in a hurry, he could use two or more rabbits and sacrifice one or more of the animals eighteen hours after the first injection. In a large number of animals the ovarian changes will have occurred by this time, for, as reported previously,⁸ even a single intravenous injection of urine from a pregnant woman can provoke ovulation in a rabbit within twelve to fourteen hours. Before the present routine was adopted, we did use the single intravenous dosage with the eighteen-hour autopsy, but found that it was not entirely reliable. Yet, in the event of necessity, this method could be employed, if one would not place too much faith in negative results. By this means crude urine may be used, thus avoiding the need of alcoholic precipitation and subsequent concentration of the active substances.

Another advantage of the method we propose is the ease with which the results can be determined. When the mouse is used as the test animal, a hand lens is needed frequently to determine the presence or absence of a positive reaction, and in about 12 per cent of the cases, microscopic study is required.¹² When the rabbit is used, the results

are perfectly apparent without the use of a lens or microscope at any time (Fig. 1).

Finally, only one rabbit need be used for each sample submitted. To perform the test of Zondek and Aschheim, five mice are prescribed for each sample because of the variability of response from mouse to mouse. Nevertheless, at the market price of \$1.60 for each rabbit, and considering that a rabbit will consume more in a month than will five mice, it is likely that the procedure we have outlined will prove the more costly. This added expense is not great, however, and we believe that the other advantages will be of more weight than this item of expense.

SUMMARY

1. A procedure is described by which the injection of urine into female rabbits may be utilized in the diagnosis of early human pregnancies.

2. The results obtained with this procedure have proved to be correct in each of the 92 cases for which we have satisfactorily complete records. To date, we have been unable to discover a single instance wherein the laboratory findings were in error.

3. The advantages of the procedure, from the standpoint of speed and simplicity, are indicated.

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THYMOPHYSIN IN SELECTED CASES OF UTERINE INERTIA*

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THYMOPHYSIN is a combination of the extracts from the thymus and from the posterior lobe of the hypophysis. For the past five years it has been used for the treatment of inertia of the uterus in many of the European clinics. A review of the literature leaves one with the impression that thymophysin has the advantage over pituitrin in that it produces labor pains of a purely physiologic type and is without harm to the mother or child.

American publications by Haynes in 1928 and recently by Jarcho and Temesvary in the *American Journal of Obstetrics and Gynecology* seem to substantiate the reports with regard to the usefulness and relative safety of thymophysin. DeLee and Greenhill, however, in the 1929 *Year Book for Obstetrics and Gynecology* warn against the use of thymophysin. They state that thymophysin is a weak pituitary extract with all the faults of pituitrin.

In studying the effect of thymophysin in treatment of inertia of the uterus, it seemed best that only those cases that presented an obstetric problem should be used. Just because labor begins with rather weak and irregular pains can hardly be considered a sufficient indication for the administration of uterine stimulants. So many factors seem to alter the character and rhythm of labor pains that all such conflicting influences should be eliminated as far as it is possible to do so.

A period of rest with morphine or chloral and bromides is often followed by the onset of satisfactory pains with the result that labor is frequently terminated within the limits of normal duration. Rupture of the membranes frequently results in the onset of satisfactory pains. Effective pains may begin following vaginal examination, especially if the cervix has been manipulated during the examination and again the onset of good pains may start for no apparent reason.

This study, therefore, has only to deal with those cases of uterine inertia in which labor is unduly prolonged and in which the above factors have been excluded.

In two hundred and twenty consecutive deliveries per vaginam, labor was unduly prolonged because of uterine inertia in six cases, which were selected for this study. The method of selection was based upon the fulfillment of the following conditions:

*Read at a meeting of the Chicago Gynecological Society, June 20, 1930.

First, that labor shall have lasted longer than ten hours without appreciable advance. During this period the pains should be of short duration and irregular in interval.

Second, that at least two hours shall have elapsed after a period of rest, vaginal examination or rupture of the membranes. At the end of this period of time the pains shall not have changed in frequency and character, and labor must be for all practical purposes at a standstill.

Third, that no disproportion shall exist between the pelvis and the fetal head.

CASE REPORTS

CASE 1.—Primipara went into labor August 9, 1928, at 4:00 P.M.; weak, irregular pains four to ten minutes, lasting fifteen seconds. Cervix well effaced, dilatation 1 cm. Weak pains continued with no progress until 9:00 P.M. Rested with morphine. Pains irregular in the morning of August 10, 1928; at 12 noon, dilatation was 4 cm., membranes were intact. At 4:00 P.M., dilatation was still 4 cm., and membranes were still intact; 10 minims of thymophysin were given. Ten minutes later strong effective pain, three minutes apart and lasting forty seconds. Heart tones were 160 and regular. At 6:00 P.M. dilatation was complete, the membranes were ruptured artificially and the position was left occiput transverse in the mid pelvis. The pains became weaker and at 9:00 P.M., little if any progress had been made; five minims of thymophysin were given and the pains became more frequent and of longer duration. At 9:30 P.M. pains were becoming less strong and the position of the head remained unchanged. At 10:00 P.M. patient delivered with Kielland forceps, left occiput transverse mid pelvis. The mother and baby were normal during their stay in the hospital and left in good condition.

CASE 2.—Primipara entered labor at 4:00 P.M., August 14, 1928; weak, irregular pains, cervix effaced, dilatation 1 cm., membranes intact. At 1:00 A.M., August 15, 1928, no progress. Patient rested with morphine and slept well for six hours. Had weak, irregular pains all day, August 15, 1928; rested by morphine at 10:00 P.M. and had four hours sleep. At 9:30 A.M., August 16, 1928, dilatation was 3 cm., membranes intact and head in left occiput transverse position; seven minims of thymophysin were given. Ten minutes later good pains, three to four minutes, lasting forty seconds. Patient delivered normally at 2:00 P.M., August 16, 1928. Mother and child normal during stay in hospital and left the hospital in good condition.

CASE 3.—Para ii entered the hospital in labor at 10:00 A.M.; had weak, irregular pains all day, cervix dilated 3 cm., position was right occiput posterior. Membranes ruptured spontaneously at 1:30 the next morning. No progress or change in character of pains at 3:30 A.M.; 7 minims thymophysin were given. Ten minutes later, good pains, two to three minutes apart, lasting thirty to forty seconds. Normal delivery, at 4:30 A.M. Child and mother normal during stay in hospital and left in good condition.

CASE 4.—Para iii; weak pains; dilatation 3 cm., cervix effaced, head in left occiput transverse position. Pains continued weak throughout the day and night. Patient rested with morphine at 9 A.M. the next morning and slept for five hours. Pains continued weak and irregular, dilatation 3 cm., membranes intact; apparently no progress; 5 minims of thymophysin were given at 2:00 P.M. with no results. Seven minims of thymophysin were given at 2:30 P.M. without apparent result in the character of the pains. At 3:00 P.M., 10 minims of thymophysin were

given and the pains became somewhat stronger but died down at 3:30 P.M. without producing any effect on the progress of labor. At 4:00 P.M. the membranes were ruptured artificially. The pains became more regular and delivery was accomplished at 11:00 P.M. after complete dilatation by Kielland forceps, left occiput transverse, mid pelvis. Mother and child normal during their stay in the hospital and left in good condition.

CASE 5.—Para iii, colored, entered after being in labor at home for thirty-six hours with membranes ruptured. After several hours of rest the pains were weak, irregular; dilatation 8 cm., right occiput transverse position. No progress for two hours. Ten minims of thymophysin were given. Five minutes later uterus went into tetany, heart tones fell to 60 per minute, meconium appeared in the amniotic fluid. Patient was put to sleep with ether and delivered with Kielland forceps. Baby was badly asphyxiated but was resuscitated. Mother and baby normal during stay in hospital and left in good condition.

CASE 6.—Primipara. On October 17, 1929 the cervix was dilated 3 cm., membranes in act, head in mid pelvis, occiput right transverse, heart tones regular and patient was having weak pains. There was no progress in nine hours. She was rested with morphine until 6:00 A.M., October 18, 1929; weak irregular pains continued, dilatation 3 cm., membranes intact. At 9:30 A.M. thymophysin, 10 minims, was given. Uterus went into tetanic contraction, heart tones fell below 100, increased fetal movements could be auscultated. Ether inhalation and morphine given to control tetany. The patient was delivered with Kielland forceps, right occiput transverse, thirty-six hours later. Amniotic fluid contained meconium. Mother and child were normal during stay in hospital and left in good condition.

Thymophysin used for the purpose of effecting satisfactory labor pains in this group of six selected cases of uterine inertia proved successful in two; aided the stage of dilatation in one, failed in one and produced uterine tetany in two.

It would seem that one would least expect uterine tetany to occur in the above cases because the uterus has contracted in such a feeble manner and does not appear to be irritable. Nevertheless, we feel that the appearance of uterine tetany is of some significance, especially when the dosage given was less than that usually recommended. At least several facts are quite evident from this group of cases. First, that thymophysin is not as reliable a preparation as one is apt to believe from the literature; second, that unless our experience is very unusual there must be similar experiences in other clinics where thymophysin has been used. We feel that the publication of our results obtained with thymophysin is indeed timely. We are not at all convinced that thymophysin is an entirely reliable and safe preparation, even in the face of an abundance of testimony to the contrary.

A NEW METHOD FOR DETERMINING THE PATENCY OF THE TUBES IN THE COURSE OF ABDOMINAL OPERATIONS*

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WHILE working with Drs. Allen, Pratt and Bland^{1, 2, 3} in a search for ova in the fallopian tubes of women, it occurred to us that the method we used, with some minor modifications, would be an ideal

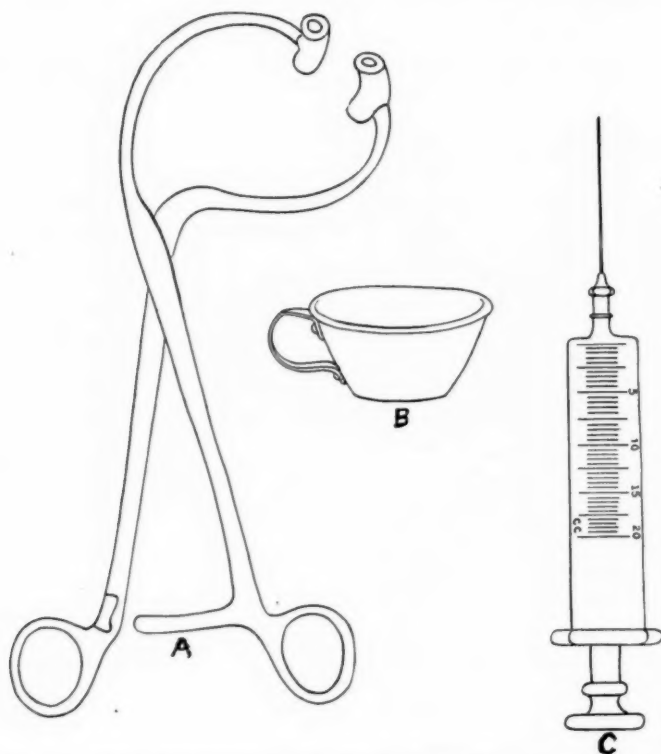


Fig. 1.—The necessary instruments for tubal insufflation when the abdomen is open. A. Uterine compression forceps. B. Cup. C. Syringe and needle.

procedure for determining tubal patency subsequent to plastic correction of obstructions revealed through a preceding hysterosalpingogram. A detailed description of the technic at present employed is as follows:

With the necessary plastic work done and intestines well packed away, a special uterine elevating forceps, the tips of which are covered

*Presented to the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Niagara Falls, Ontario, September 15, 16, and 17, 1930.

with rubber tubing to avoid any injury, is placed on the uterus from above downward, shutting off the cervix at about the level of the internal os (Fig. 1). This forceps is curved and is held forward by the first assistant. With thumb and index fingers of the other hand, this assistant compresses the tube on the side opposite the one to be tested for patency. The second assistant holds a small aluminum cup, 6 cm. wide and 3 cm. deep, having a handle for convenience (Fig. 2), underneath the fimbriated end of the tube to be tested to catch carefully all

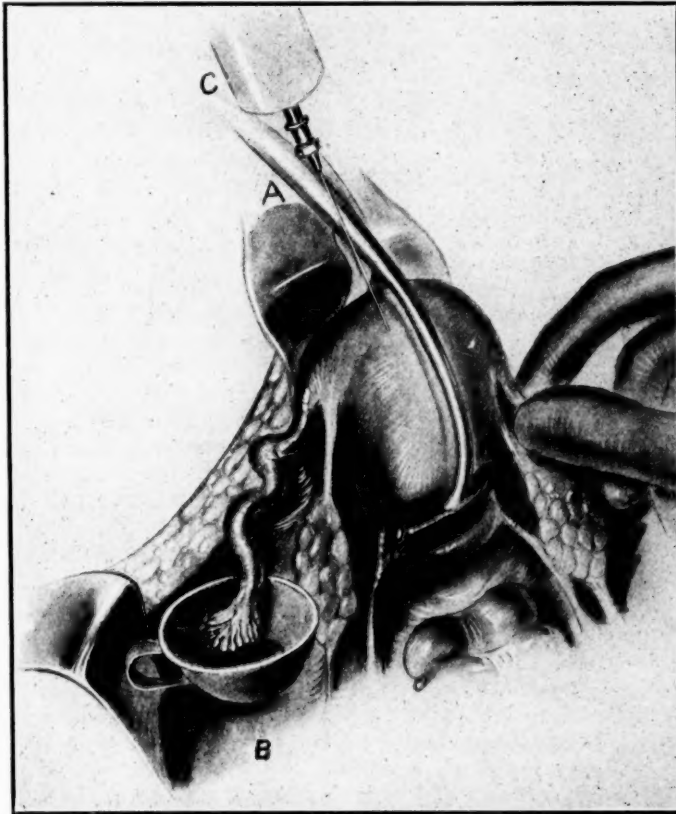


Fig. 2.—A drawing showing the method in operation. A. Uterine compression forceps. B. Cup. C. Syringe and needle.

of the passing irrigating fluid. A small calibered needle attached to a 20 c.c. syringe is pushed through the fundus into the uterine cavity, entrance into it being clearly perceived by a sudden cessation of resistance. Normal saline solution is then slowly injected. The uterus is filled up and gradual distention of the tube to be tested is observed to progress from the uterine toward the fimbriated end, granted the tube is patent. Several syringes full of fluid should be used for thorough irrigation since there is a possibility that this irrigating process might have some therapeutic effect.

This method has been used by me for the past two years and in no instance was any injurious effect noticed. I consider this method safer than similar procedures which unlike this one cause the injected material to enter the free abdominal cavity. The only contraindication would be an active infection in either uterus or tubes, but as a matter of fact under these conditions the operation for removal of a visualized obstruction should not have been attempted.

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411 WALL BUILDING.

Gibberd, G. F.: A Contribution to the Study of the Maternal Death Rate. *Lancet* 2: 535, 1929.

The cases studied are divided into those occurring from 1863 to 1875, and 1919 to 1928, the two groups showing the comparisons of the midwifery of these periods.

The maternal mortality rate has fallen from 4.4 to 1.03 per 1000. Simultaneously there has been a steady increase in interference, but it is still less than 9 per cent. Improvement in aseptic and antiseptic technic has contributed much, particularly with the increased interference.

Antenatal care has its greatest value in reducing death in cases of disproportion and malpresentation, and in limiting the number of eclamptics along with the opportunity to prepare the patient to better face the risk of labor and the puerperium.

The concealed hemorrhages take about as many now as sixty years ago, while in cases of external hemorrhage a reduction in death rate has resulted principally from the use of saline, gum saline, and blood transfusions in conjunction with measures to combat the cause of hemorrhage. In toxemia, the greatest stride has been made in prevention and less in cure.

The intercurrent diseases took 0.32 and 0.24 per 1000 in the two respective periods.

H. C. HESSELTINE.

Society Transactions

AMERICAN ASSOCIATION OF OBSTETRICIANS, GYNECOLOGISTS AND ABDOMINAL SURGEONS*

FORTY-THIRD ANNUAL MEETING

NIAGARA FALLS, CANADA, SEPTEMBER 15, 16, 17, 1930

THE PRESIDENT, DR. EDGAR A. VANDER VEER, IN THE CHAIR

DR. I. W. POTTER, Buffalo, N. Y., Chairman, read a **Report of the Committee on Maternal Welfare**. (See page 290, February issue.)

ABSTRACT OF DISCUSSIONS

DR. A. M. MENDENHALL, INDIANAPOLIS, IND.—The preliminary figures as presented by Dr. Potter are indeed very discouraging. If we simply analyze those figures as presented in the first few pages of this paper, we cannot feel at all satisfied with the efforts we have been making in the past few years and are contemplating doing in the near future. But I am more optimistic than that. I have a feeling, in the first place, that prenatal care is eventually going to accomplish much more than it has in the past. The most encouraging statistics are those showing how much better the women have been who have had prenatal care.

I also believe that extension courses in certain States offer a good outlook in carrying the message of better obstetrics to the practitioner. This is more practical than expecting them to attend the state and national organizations. Naturally, we shall not feel the results of those things for years to come, but it is definitely worth while. At the White House Conference it was well said that we might teach obstetrics almost perfectly and yet, when the men leave the hospital they soon gravitate to the type of obstetrics done by the men who have been out longer, unless we continue to carry the teaching of better obstetrics to them and impress upon them the necessity of continuing it.

I have a feeling that marked progress is being made in the teaching of obstetrics and that our former President Findley's paper did much good. It has gone out to state organizations and most of our state journals reviewed it, giving the man in general practice an opportunity to see what is needed in obstetric teaching. In Indiana in the last two or three years we have practically doubled the hours that were allowed to obstetrics. Formerly surgery had the greater number of hours but now obstetrics is on practically an equal basis with surgery and we are hoping it will soon be on an equal basis with general medicine. A great aid to better obstetrics practice will follow without doubt, when the newly developed Board of Obstetricians and Gynecologists has become organized to the point of examining men for their qualifications in this speciality. Many now take a very short course in postgraduate obstetrics and then call themselves obstetricians. Obviously this Committee cannot overcome all of those obstacles, but I believe it will eventually do great good.

DR. JAMES R. BLOSS, HUNTINGTON, W. VA.—It is a matter of disappointment to those of us who are giving our attention to obstetric work to know that

*The current volume of the Association Transactions will contain the complete discussion which cannot be presented here for lack of space, as well as those papers which were unsuited to the pages of this JOURNAL because of their purely surgical character.

there has been no improvement shown in the maternal death rate. It would seem that our efforts so far have not been productive of the improvement which we have been so earnestly striving for. The report of the Committee, however, very clearly brings out that we can do much to improve these conditions if we can only secure the cooperation of the prospective mothers with the physicians. The figures given in the report from the Report of the London East Side Maternity Hospital, and that of the Maternity Center Association, together with the Metropolitan Life Insurance Company, demonstrate where the trouble probably exists. It would seem, then, that our greatest effort should be extended toward educating the laity in regard to the importance of prenatal care.

There seems to be gradually growing the realization in the medical profession that the subject of obstetrics has not been given the proper amount of time in medical schools. Probably obstetrics has suffered in the curriculum because of the idea of the importance of the other fundamental branches of practice. It is a question as to how much this is affected by the financial returns from this branch of medical service. In the past it has been believed that anyone could deliver a woman, not realizing that obstetrics is the most important specialty in all of medical practice, and the poorest paid. As physicians in practice we can realize why the present status of obstetric service obtains. If the laity would be satisfied with the same brand of surgery, or the services of internists no better trained, then these branches would not make a showing any more commendable than the one brought forth by the study of these statistics. I do believe, though, from my contact with interns who have come more or less under my observation and supervision during the past two or three years, that they are giving evidence of better instruction. It seems that their obstetric conscience is better developed, and that they have a better foundation in the fundamentals of obstetric practice.

I heartily approve of the postgraduate courses which are being instituted at various points throughout the country. It seems to me that this Association should encourage this in every way.

The report of the Committee calls especial attention to the opportunity presented for us to get the maternal welfare idea to the laity when it deals with the question of interesting Parent-Teacher Associations and Mothers' Clubs. It seems to me that we have been overlooking a golden opportunity to get this educational work across. It is a very difficult thing, however, for a physician in a community to push himself forward and attempt to appear before these organizations. Surprising as it may seem, the other physicians in his locality belittle his efforts and make light of his attempt to better conditions. Immediately his confreres accuse him of advertising and of being unethical. We can readily understand that a sensitive physician with ability hesitates to subject himself to these unpleasant comments. As we know, generally the most competent men are the most retiring and least inclined to advertise in any way, and usually it results in the speakers being those who have not given the most thought to the subject.

So, in conclusion, it would seem that the most important thing at the present time is for this Association to have its committee give special attention to devising ways and means to bring before the laity the great importance of prenatal and postnatal care.

DR. BENJAMIN CARROLL, TOLEDO, OHIO.—For some time I have had in mind two suggestions along the same line of thought as that offered by the Committee. The first will aid in studying the cause and the second will help in lowering our maternal and fetal mortality rate.

First, at present, methods of arranging hospital statistics are not satisfactory and not entirely adequate. I would suggest that this Committee arrange a standard statistical form to be used by all hospitals, this form to be filled out for all pregnant women as they enter the hospital and again to be rechecked when the patient is dis-

missed; these daily or individual forms to be tabulated into a monthly report and monthly reports compiled into a yearly report. The hospital librarian, under the direction of the Chief of Obstetrics, shall be responsible for this data. By such a method of collecting statistics we would have readily available a uniform report from all of our hospitals. From such a report each hospital could make a comparative study of its own standing and would be stimulated toward more careful work.

My second suggestion is that a definite plan leading to a division of hospital obstetrics into major and minor cases be inaugurated by the Maternal Welfare Committee or a subcommittee. By comparison we have today as many good obstetricians in the communities surrounding our hospitals as the College of Surgeons had surgeons a few years ago when they reorganized the practice of surgery in the hospitals. (We also have as many inefficient men.) Last year in the cities approximately 50 per cent of the babies were delivered in the hospitals. Our mortality rate remains high. Not until our obstetric practice is on a plane equal to or higher than that of surgery will our hospital death rate be lowered. One, if not our foremost, duty as obstetricians is to make all of our hospitals "a safe place for confinement."

There are two other very good reasons for organizing hospital obstetrics. First, the interns, who in the past two or three years have shown a marked improvement in obstetric knowledge, are in these hospitals for their training. We must continue to impress upon them the importance of the abnormal obstetric cases. The second benefit of organized hospital obstetrics would be in paving the way and making a place for the new men, who have put in several years of intensive obstetric study.

DR. CHARLES S. BACON, CHICAGO, ILL.—The basis of the report, and of all our discussion is, statistics, and the importance of correct statistics is therefore great. Now it is impossible to get correct statistics unless there is uniformity in the records of different places and everything depends first upon the definitions, and second upon the carrying out of the rules of the statistics bureau of the community in which the records are kept. The definition of living birth is of the greatest importance. In many places the rule that every birth shall be called a living birth if there is any sign of life after delivery is followed; in other places a birth is not regarded as a living birth if there is simply action of the heart but no respiration.

The records in many places should, if made according to the direction of the office, include as living births children born after more than five months gestation showing any sign of life. In a hospital with which I am connected we carry out this rule. Every patient that is delivered where the duration of pregnancy is over five months, and where there has been any sign of life, is stated to have had a living birth. Necessarily we have a rather high fetal mortality because of that fact. It seems to me absurd to call a nonviable child a living child for the purposes of statistics, and efforts have been made by the Committee of the League of Nations in Geneva to bring about uniformity in definitions of living and dead births.

DR. JOHN O. POLAK, BROOKLYN, N. Y.—We are convinced from the work which we have been doing on the White House Conference that the conditions in obstetrics are deplorable. It seems to me the point which we made some time ago should be emphasized, i.e., that all of this prenatal work is wasted money and time unless it is followed by consecutive, intelligent, aseptic obstetrics based upon a knowledge of the obstetric art and an obstetric conscience. There is something more to obstetrics than a clean hand and a sterile knife. This is brought home to me in an article published by the State Board of Health in Massachusetts, analyzing 370 primiparous obstetric deaths. Among the 370 patients 101 had cesarean section and over 50 of them died from peritonitis, embolus, shock, and hemorrhage. This means lack of obstetric conscience and if this Association hopes to accomplish any-

thing, it must begin, as has been suggested, to train our interns not only in the details of obstetric practice but also in their relation to the patient.

Many of these deaths are due to sepsis and toxemia, two of the supposed preventable conditions. If we go through any more statistics it will be seen that there has not been an appreciable decrease, notwithstanding the propaganda which has been circulated in the past few years. We must go further and educate our public to a demand for better obstetrics, and do not forget that the doctor, no matter what amount of prenatal work he is doing, must follow it by intelligent delivery care.

DR. FRED L. ADAIR, CHICAGO, ILLINOIS.—The Joint Committee on Maternal Welfare was originally formed following a request from the American Child Health Association, consisting of three members each from this Association, the American Child Health Association, and the American Gynecological Society. There has been added to the membership the section of Obstetrics, Gynecology, and Abdominal Surgery of the American Medical Association. Many of the members of this Joint Committee have been very busy at the White House Conference, so that they have concentrated practically all their efforts in that direction. However, I believe that by close correlation and cooperation between the different communities we can accomplish much more for maternal welfare than by the activities of any committee representing only one organization.

DR. JAMES E. DAVIS, ANN ARBOR, MICH.—I wish to make two practical suggestions concerning the control of statistics and the study of the pathologic features that occur in this work. In each hospital when a junior member of the staff is appointed to the Department of Obstetrics and Gynecology, he should be given the responsibility of looking after the department's statistics. Before the record becomes a permanent item of the file it should be reviewed carefully to see that it is an available and useful record. Furthermore, the junior member of the staff ought to be capably trained in pathology. A large percentage of the members on the staffs of the larger hospitals are wholly incapable of reading gross specimens or microscopic sections. Appointments to the staff should, therefore, have adequate preparation for this work.

SYMPOSIUM ON THE HEMORRHAGES OF PREGNANCY

Management of the Third Stage of Labor, With Special Reference to Blood Loss, by DR. L. A. CALKINS, Kansas City, Mo. (See page 175, February issue.)

Placenta Previa, by DR. A. H. BILL, Cleveland, Ohio. (See page 227, February issue.)

Hemorrhage in the Early Months, by DR. W. B. HENDRY, Toronto, Canada. (See page 211, February issue.)

Accidental Hemorrhage, DR. J. O. POLAK, Brooklyn, N. Y. (See page 218, February issue.)

DISCUSSION

DR. I. W. POTTER, BUFFALO, N. Y.—I am inclined to doubt that the length of the second stage of labor does not increase the fetal deaths. The first stage of labor, it seems to me, has no effect whatsoever upon the patient.

The thing that impresses me in regard to blood loss in the third stage of labor is the location of the placenta. If the placenta is attached to the fundus of the

uterus, the blood loss is reduced to a minimum. If, however, it is attached to the uterine wall or comes into the group of previas, then the blood loss increases just in that proportion, regardless of whether the patient is treated or not.

Interference with the third stage of labor induces trouble, because it causes a greater blood loss, opens up avenues for infection, and leads one into considerable danger. If, however, immediately upon the separation of the placenta, it is removed from the uterus before it becomes a source of irritation, then the blood loss is again diminished.

In our experience we have not found that the blood loss in the third stage of labor has been increased by the general anesthetic. We use chloroform altogether. Pituitrin given after the birth of the child is routine treatment.

It seems to me that the size of the child can very easily increase the blood loss during the third stage. With a large child the tissues are more or less devitalized and the blood loss is greater in that case. The method of delivery has also something to do with the blood loss. I am speaking now from practical experience, but we do know that in a long, tedious second stage the blood loss is greater than when the second stage is shortened by immediate delivery of the child.

Regarding Dr. Bill's paper, there is only one suggestion that I would like to make—I would include placenta previas under one heading and not have three divisions. If it is a placenta previa, it is a placenta previa and is an operative case.

DR. G. D. ROYSTON, ST. LOUIS, MO.—Among 13,182 hospital admissions in the Washington University Clinic, there were 37 cases of placenta previa, 18 undoubted instances of premature separation, and 60 classified under accidental hemorrhage. A study of the history records of this latter group disclosed many with low-seated placenta, cervix eroded or traumatized during previous labors; others who had protracted general narcosis followed by atonic uterine contraction, etc. No doubt there were many instances of premature separation of slight degree that had escaped notice, but only those patients with symptoms resulting from a separation were so classified. I feel that there is too much guesswork in studying the placenta and attached clots with no exact knowledge of the cervix and lower uterine segment, to enable one to make a positive diagnosis.

Among 125 patients with eclampsia or preeclamptic toxemia, no instance of ablatio occurred.

DR. FRED L. ADAIR, CHICAGO, ILL.—The management of these bleeding cases is necessarily complicated by considerations due to the maternal life and health and that of the fetus in utero, except where the offspring is already dead or previable. Even in uterine bleeding in the early months of gestation one is actuated by a desire to preserve the embryonic and fetal life in the management of threatened abortion. The treatment of threatened previable terminations of pregnancy with bleeding is to carry on to the period of viability if it is consistent with the health and life of the mother, by complete rest, with the administration of opium or morphine and belladonna or atropine, all under supervision and control of the patient in appropriate surroundings. When the process becomes inevitable, the uterus should be encouraged to empty itself, but great caution must be used in the employment of artificial means in potentially and actually infected cases. If the bleeding necessitates intrauterine manipulations, they should be carried out with great gentleness in an effort to avoid breaking down the natural barriers to infection. In noninfected cases the uterus may be artificially emptied with relatively little danger, though instrumentation of any pregnant uterus is fraught with the danger of serious trauma.

Under ideal conditions, with a properly equipped maternity hospital and competent personnel, a section is a desirable procedure in properly selected cases of

placenta previa but it is probably not needed in all. In the vast majority of cases such ideal conditions are not at hand and other methods must be used.

The obstetrician must avoid provoking any bleeding by rectal or vaginal examination until everything is ready to proceed in accordance with an outlined plan to control bleeding and secure cervical dilatation. If possible, all of these cases should be adequately hospitalized. Haste in delivery through inadequately prepared passages is to be rigorously avoided.

I will quote a few statistics from the Chicago Lying-In Hospital. There were 144 cases of placenta previa in approximately 15,000 deliveries. The incidence of cesarean section of various types in these cases was 42, or approximately 29 per cent. There were two maternal deaths in the series, which makes the maternal mortality from placenta previa about 0.75. Neither of these deaths occurred in a mother who had a cesarean section.

Among the 15,000 cases at the Chicago Lying-In Hospital mentioned above there were 113 cases of abruptio placentae. There were five maternal deaths which make a maternal mortality of 4.4 per cent. In this series there were 26 cesarean sections of different types, a percentage of 23.

DR. E. D. PLASS, IOWA CITY, IA.—Dr. Calkins was unable to utilize my cases in the determination of the effect of parity upon the amount of postpartum bleeding. These figures have been analyzed and show that, while there is no difference in blood loss in the average patient, multiparity does increase the chance of a postpartum hemorrhage with a blood loss of 600 c.c. or more.

Among 613 primiparous women in my series, there were 38 or 6.2 per cent, who lost 600 c.c. or more of blood, while among 557 multiparas, 64, or 11.2 per cent suffered a postpartum hemorrhage according to the criteria.

I would like also to emphasize that the kind of anesthesia employed has an effect upon the blood loss. Some years ago we reported upon the apparent effect of ether, either alone or in conjunction with another inhalation anesthetic, in promoting bleeding. Further experience has confirmed these observations. Our recent experience with chloroform has been too meager to permit conclusions to be drawn concerning its effect, and the newer agents have not been studied with this in mind.

We have held that the use of transfusions to combat the blood loss and shock in patients with placenta previa is the essential feature of the treatment, believing that if the patient is restored to good general condition, treatment either with the bag or by cesarean section will be satisfactory. My personal objection to the employment of abdominal delivery is that advanced against its use in all incidental indications—the same operation will be done in each succeeding pregnancy even when there is no indication other than the previous operation.

DR. J. C. LITZENBERG, MINNEAPOLIS, MINN.—This is an age of prophylactic thinking. The paper of Dr. Calkins, read this morning, directs itself to the prophylaxis of the loss of blood. We should cease thinking of obstetric cases in terms of mortality, or we might go even further and think in terms of the physiology of the woman, the slight disturbance of her health. It would seem unnecessary to argue before this audience that the conservation of every ounce of blood possible will lead to a more rapid recovery and the more certain return and maintenance of health.

As surgeons we emphasize a delicate handling of tissues. That often is the mark that distinguishes the expert surgeon from the mauler and that has to do with the health of the individual. We no longer operate in a sea of blood, but try to conserve every drop of blood possible.

Dr. Calkins did not tell you that the average loss of blood in his cases was 200 c.c. All of Dr. Plass's cases were privately conducted and the loss of blood

was 290 c.c. Our average loss of blood at the Minnesota Hospital is 450 c.c. I consider 300 c.c. as a postpartum hemorrhage, either that some accident has occurred beyond my control or I have not handled that case properly. I commend the technic which has been spoken of. Perhaps the bleeding in our clinic at the University of Minnesota more nearly approaches the average private case. Our cases are handled either by the resident or an intern. If we call ourselves expert obstetricians, I do not believe we should have a loss of over 300 c.c. of blood, and our figures for postpartum hemorrhage should be lowered, in general, at least from 600 to 500 c.c., and in the hands of experts to 300 c.c., unless the hemorrhage is due to something beyond our control.

In teaching students the Credé method correctly one must insist that the hand be placed behind the uterus as far as possible, with the thumb in front, and the uterus squeezed and not pushed. That eliminates the danger of pushing the cervix down where it may become infected. In this technic it is ever necessary to keep in mind that massage, unusual massage particularly, should not be used.

DR. JOSEPH L. BAER, CHICAGO, ILL.—I should like to outline for you the successive procedures tried out in the treatment of the third stage under my observation at the Michael Reese Hospital from 1904 to 1930. I was taught to hold the uterus for one hour after the end of the second stage whether placenta had been delivered or not. For one hour either the intern or the nurse had to hold the uterus, massaging as they saw fit for softening or bleeding. Then that period was cut down to thirty minutes during which no attempt at expression could be made. At the end of the thirty minutes the placenta was to be expressed or delivered by the Credé method if it had not come away spontaneously. Then in 1919, after we had run out of ergot because of the War conditions, we stopped the use of ergot which heretofore had been routine; we found that there was no difference in the third stage bleeding without the administration of ergot, so we permanently omitted the routine use of ergot. Then in 1925, following a presentation by Dr. Danforth on the routine use of pituitrin, we began using that, one-half ampule at the end of the second stage, and one-half ampule after the placenta had been delivered.

During these last years, however, we have completely discontinued holding the uterus. For a period of ten years we placed the hand across the abdomen in diaphragm fashion above the uterus without holding it, merely touching it to give us contact information. That was initiated when we used pituitrin.

In 1918, during the period of holding the uterus and giving ergot routinely, in 1,000 consecutive cases the average length of the third stage of labor was twenty-seven and a half minutes; in 1930, in 1595 cases, without touching the uterus except to determine its consistency, and with the use of pituitrin instead of ergot, the average length of the third stage was nine minutes. In 1918 we

TABULATION OF THIRD STAGE DATA DURING 1918 AND 1929

1918		1929
	<i>Duration of Third Stage</i>	
27.5	Average	9.2 %
97.1%	Less than 30 min.	98.4 %
2.9%	Over 30 min.	1.6 %
	<i>Hemorrhage</i>	
3.0%	Slight and moderate	2.92%
0.3%	Severe	0.26%
3.3%	Total	3.18%
	<i>Placenta</i>	
0.9%	Manual removal	0.94%
0.5%	For hemorrhage	0.5 %
0.4%	Adherent	0.44%

did not do any manipulating to force the placenta out. We simply held the uterus for thirty minutes, whether the placenta appeared at the vulva or not, and at the end of thirty minutes expressed it.

We are almost convinced now that the routine use of pituitrin is superfluous and makes no real difference in the loss of blood in the third stage.

I believe that holding the uterus, likewise is totally unnecessary and frequently harmful, because holding the uterus before the placenta has been separated not infrequently includes massage for the softening of the uterine wall which is really normal relaxation, and results in irregular separation of the placenta with resultant increased bleeding and retention of a partially adherent placenta. Holding the uterus after separation is certainly superfluous because, so far as we can determine, it plays no part in the control of blood loss. Separation is the important consideration in the third stage. This can be determined without holding to the uterus. Frequent palpation is better and safer. Bleeding from the vulva is valuable evidence. We tie a bit of tape on the cord, and the advancement of that mark is another very good index. Again, the alteration of the contour of the fundus is significant. As it rises and becomes conical, it shows that the placenta has moved down into the lower uterine segment.

I believe that in the majority of instances there is no need for expression after the placenta has separated. If the woman is awake and of a cooperative nature, one need merely pull the recti together above the fundus in the upper abdomen, thus reconstructing the intraabdominal pressure at the height of a contraction, and in 90 per cent of our series the patient expels her placenta, using her uterus as the piston to drive the placenta out of the birth canal. I described that procedure eleven years ago. It has won very general recognition on the Continent and is used in Western Europe quite routinely. Its acceptance has been a little slow in this country, perhaps because many of our patients in the third stage are under the influence of a drug or anesthetic.

If I may say one word more in discord, I cannot agree with classifying placenta previas as placenta previas and nothing else. Neither can I agree with the complete omission of vaginal examination on hospital patients. In a long series of vaginal and rectal examinations Dr. Ralph Reis, of our clinic, found that the morbidity at the end of the complete series was identical. We have no fear about doing a vaginal examination on admission to determine the *status praesens* of the patient whom we are considering. We do prescribe that a woman who is bleeding when admitted to the hospital shall not be examined by the house staff. A member of the staff is always available to do vaginal examinations, and I cannot agree that in a multipara, in whom the placenta is situated very eccentrically, as revealed by vaginal examination, it would be justifiable to deliver her by an abdominal operation. Simple rupture of the membranes, not to reenumerate the other procedures, has more than once closed the whole chapter of a placenta previa without any further intervention. Why do a section on that type of patient?

DR. ALEXANDER M. CAMPBELL, GRAND RAPIDS, MICH.—We employ a very simple method of preventing excessive hemorrhage by tamponade of the uterus. For the last two years we have been doing routinely immediate repair of the cervix following labor, and in working out this technic it occurred to me what a simple thing it is to pack carefully a bleeding uterus when one uses the DeLee vaginal retractors and proper tenacula. I maintain that if proper care is taken and if this technic is followed, there is practically no danger of infection. We have used this method in a sufficient number of cases without the slightest morbidity. We believe that careful tamponade of the uterus is much preferable to, and much more effective, than the forcible massage which is so often used in an attempt to control excessive postpartum bleeding.

Concerning placenta previa, I want to state that, as a practitioner who has followed the statistics on cesarean section for many years, I am glad that there are other members of this Association who do not take such a radical attitude as to advise cesarean section in every case of placenta previa. I think every such case is a law to itself and I am convinced that some cases will deliver themselves spontaneously and safely and that a number of cases may be successfully delivered by the use of a dilating bag.

I will admit that cesarean section is a procedure of choice in many cases when it can be done by a skillful operator and under favorable circumstances, but I think that the statement that every case of placenta previa should be submitted to cesarean section is a very dangerous one to emanate from this Association.

DR. W. S. BAINBRIDGE, NEW YORK CITY.—I am wondering whether in considering the question of hemorrhage, we have taken into consideration the physiologic chemistry of the blood? Where it has been possible, I have tried for years to get the coagulation time of the blood, and where possible, also the calcium content, although the coagulation time carefully done will give us a general rough view of the physiologic element in relation to coagulation. If the coagulation time is from seven to fifteen minutes, a few days of adequate medication will safeguard the patient and diminish hemorrhage. I question whether we are not often derelict in not paying more attention in our surgical work to blood chemistry.

DR. C. R. HANNAH, DALLAS, TEXAS.—I was particularly impressed with the discussion of Dr. Baer. Whenever we think of labor, we think of uterine contractions and these contractions are present through the first, second, and third stages of labor. I have observed often that a patient will complain of painful contractions during the third stage of labor almost equal to those of the first stage. These contractions of the third stage are of such severity at times that an anesthetic is necessary for relief. These painful contractions may mislead us, and cause the attending obstetrician to attempt to express the placenta before separation. The third stage of labor should be thought of as of two stages: first, separation; second, expulsion. An attempt should not be made to express the placenta until it is separated, which is recognized by the ascension of the fundus of the uterus near the diaphragm, inasmuch as this maneuver will increase the loss of blood. Rough manipulation of the uterus produces bleeding. Unless pathologic, the third stage should not be hurried if we desire to prevent the loss of blood. After separation of the placenta, and during a contraction, place the palms of the hands over the recti muscles, which act as a support, and have the patient bear down; thus the placenta is expelled without an unusual loss of blood. Pituitary extract is not indicated in a normal third stage of labor; but, if given, it should *follow* the expulsion of the placenta in normally conducted cases of labor.

DR. ALONZO K. PAINE, BOSTON, MASS.—For a number of years the Section of Obstetrics and Gynecology of the Massachusetts Medical Society has been studying maternal mortality in Massachusetts; the statistics indicate that next to sepsis, hemorrhage is responsible for the largest number of maternal deaths, and that in these hemorrhage cases the placenta previas play a conspicuous part. I am especially interested, from the standpoint of teaching, in the adoption of a more or less standardized treatment for these placenta previa cases. I was glad to hear Dr. Bill minimize the importance of the variety in a given case. Dr. Potter puts it strongly when he says there is only one variety of placenta previa. It also seems to me that the wisdom of vaginal examination in these cases before the onset of labor is open to question. The existence of placenta previa can usually be established without such an examination, and the additional knowledge secured is of doubtful value in many cases; valuable time may be lost and hemorrhage increased by the procedure.

For a number of years in teaching I have emphasized two things as important in determining procedure; the symptom itself, bleeding, and the time of its occurrence. In a general way, if definite bleeding occurs before the onset of labor, the case is a potential cesarean. If this symptom appears in the seventh or eighth month, is slight in amount and ceases quickly one is justified, with the patient in a hospital bed, in waiting from day to day until the baby is reasonably viable. Recurrent flow indicates the unwisdom of further delay and a cesarean should be done. Procedure, when bleeding begins after the onset of labor, depends on the degree of dilatation of the os. If there is slight or no dilatation, cesarean section still is the procedure of choice. If the os is sufficiently dilated to permit the easy introduction of a bag, it seems the conservative procedure. If a considerable degree of dilatation is present, simple rupture of the membranes will often suffice to control bleeding. In cases where complete dilatation is easily secured, its completion manually, followed by immediate extraction, is good treatment.

DR. D. L. JACKSON, BOSTON, MASS.—Whether or not we believe in the routine use of pituitrin in the third stage, whether or not we believe in holding the fundus of the uterus, it is true that some uteri do not contract well after the placenta is delivered. In these cases where relaxation is present and bleeding is alarming, I have found that the use of pituitrin intravenously, in two or three minim doses, acts miraculously, clamping the uterus down tightly, almost before the administering syringe can be laid down and the hand returned to the fundus.

The second point I wish to emphasize is the value of getting the patient's legs out of the stirrups and getting her flat as soon as possible after delivery. This simple maneuver accomplishes the very thing Dr. Calkin mentioned; viz., it causes the uterus to come out of the pelvis up into the abdominal cavity.

DR. A. J. RONGY, NEW YORK CITY.—Bleeding toward the end of gestation must be considered in the light of a displaced pregnancy and ought to be treated as such. A misplaced nidation during the early period of gestation leads to an ectopic pregnancy. A misplaced nidation in the last six weeks results in a placenta previa. In either instance occasionally the patient may be able to get along without surgical intervention, for tubal abortion may take place and the patient gets well; the same happens in a large number of cases of placenta previa: labor sets in, the presenting part presses on the abnormally situated placenta, bleeding is controlled in that way, the child is born, and the placenta delivered with very little complication. However, placenta previa causing bleeding before the woman is in labor, before there is any dilatation, the cervix still rigid, and no presenting part to press upon the placenta, must be viewed in the same light as an unruptured ectopic pregnancy. In these cases the safest method of delivery for both mother and child is cesarean section.

During the third stage of labor, the variation in the quantity of blood lost depends to a large degree upon the coagulability of the blood of the particular patient, for in addition to the closure of the sinuses of the uterine surface at the placental site, it is also necessary that coagulation take place at the opening of those sinuses, and the sooner that takes place the sooner will bleeding or oozing cease.

DR. FOSTER S. KELLOGG, BOSTON, MASS.—It seems to me we should be slow to accept chronic nephritis as the etiologic factor in ablatio in as high a percentage as Dr. Polak suggests. Williams states in the new edition of his textbook that he saw but two cases in his series of 57. In our series we have been unable so far to establish a single case of certain chronic nephritis by interval study. Autopsy material carefully studied in relation to the kidney is very scant. We have finally in one instance found a kidney with infarct formation with desquamation of the tubular epithelium beyond. This is the picture of the characteristic

pathology of the liver in eclampsia. It also accounts for the characteristic picture of the detritus-filled tubules with attempts at epithelial regeneration described by Couvelaire and seen by us, and called by Mallory "late tubular nephritis." In contradistinction to Williams we have found in one autopsy in a patient who did not have convulsions, typical eclamptic liver lesions. We have reported eight cases (now ten) in which separation occurred on or about the time of the disappearance of albumin and elevated blood pressure in patients with nonconvulsive toxemia. Further, we reported five cases of ablatio associated with convulsive toxemia and called attention to the fact that each had one or more convulsions prior to placental separation.

DR. E. L. CORNELL, CHICAGO, ILL.—I want to emphasize the fact that we so seldom treat these hemorrhage cases prophylactically. We should give the pregnant woman, as part of her prenatal care, calcium in some form during the latter months of her pregnancy. Today most women are delivered under some form of anesthesia, either ethylene, nitrous oxide or ether; therefore the uterus at the last end of the second stage does not contract as readily as it would without any anesthetic.

A third factor, which plays an important part is the rapid delivery of the body, after the head is born. The uterus loses its opportunity to contract and retract.

Another detail in the management of the third stage is that the patient should have from $7\frac{1}{2}$ to 20 minims of pituitrin as soon as the head is born and before the shoulders are delivered. During the war we were unable to obtain packing material, so we instituted the use of pituitrin in the beginning of the third stage or at the end of the second stage of labor and since then postpartum hemorrhages have markedly increased.

I know of no way to predetermine the amount of blood any one individual will lose in any type of placenta previa; therefore, I agree with Dr. Bill that until we are able to predetermine the amount of bleeding in any patient, the cesarean section in cases with a closed cervix offers the best results.

DR. ALBERT MATHIEU, PORTLAND, ORE.—The completion of the third stage of labor does not preclude the possibility of hemorrhage. I think the patient should be left in the delivery room one hour following delivery; that the uterus should be watched, not by the one who is cleaning up the delivery room, but by one designated for that purpose; and that the doctor should stay in the hospital for one hour following delivery. I know of two deaths that might have been prevented had the patients been watched in this way, and I think I have on two occasions saved the life of a patient by being in the hospital when the hemorrhage began.

DR. JAMES K. QUIGLEY, ROCHESTER, N. Y.—There would seem to be one other reason for not packing the uterus; namely, the development of a chronic endometritis and separation of the placenta in these cases in subsequent pregnancy. I believe in packing the uterus rarely and we should pack through the large Harper tube whereby the gauze at no time comes in contact with anything except the uterus.

DR. CALKINS (closing).—I would say to Dr. Bainbridge that we have routinely taken the coagulation time for several hundred cases and so far it has been found to have no effect on the blood loss. We have not routinely made blood calcium determinations but we do routinely give calcium to all of our patients.

Dr. Hannah called attention to the manner of giving pituitary extract. We never give it until after the placenta is delivered; therefore, we do not give it in the third stage but at the completion of the third stage.

I am very glad that Dr. Baer sounded a discordant note. He pointed out that the alteration in contour of the uterus is an important sign of the separation of the placenta from the uterus. I should like to ask whether he can *see* that contour, or does he *feel* it with his hands? Ahlfeld, years ago, called our attention to the fact that only 14 per cent of all women would spontaneously express their own placentas. He had a series of several thousand cases. Williams has repeatedly called attention to that fact in each edition of his textbook.

In justification of the technic recommended for the management of the third stage of labor I would like to call attention to the fact that our figures are based on *measurement* (not estimation) of blood loss, 210 c.c. being the average blood loss, including all cases. For example, we had one patient with 2500 c.c. of blood loss in the uterus, in a case of ablatio placentae. That case is included in the average. The average is little more than one-half of the smallest previously published average. The smallest was that of Williams in the Hopkins clinic, 343 c.c. in 1000 cases. The other averages have been 500 c.c. or more.

It is a fact that too much anesthesia will produce more blood loss, regardless of the agent used. It is also true that ether will produce more bleeding than nitrous oxide, and that ethylene will produce more bleeding than nitrous oxide. Lacerations or operative procedures of any sort will increase the amount of bleeding. Hydramnios, twins, placenta previa, etc., increase the bleeding. I was considering the variation in blood loss in normal labor primarily.

DR. BILL (closing).—By way of general discussion, fifteen years ago, in a paper prepared for the Ohio State Medical Society, I advocated the routine use of pituitary extract in the third stage of labor. We have used this routinely ever since, in probably more than 40,000 cases. We have had no trouble from it whatever. Our feeling is that there is no single thing that has done as much in preventing postpartum hemorrhage as the routine use of pituitary extract as soon as a child has been born. We give a full cubic centimeter at this time.

In regard to my own paper, let me again emphasize that of first importance is the examination of the patient's condition by careful blood examination and blood pressure reading, to determine whether she is a fit subject for delivery. If she is not, a sufficient blood transfusion should be given her to make her a fit subject. We have given as high as 2200 c.c. in a single case.

As to the examination, I believe that absolutely nothing can be gained by vaginal examination. One discussant said it was radical to do a cesarean in a "supposed" case of placenta previa. It is possible to make a diagnosis of placenta previa without examination. Our comparatively low incidence of placenta previa, one in 330 cases, is proof enough that none but real cases of placenta previa have been treated in this way. Further, you must realize that vaginal examinations only add to the danger of infection and that manipulation often causes serious hemorrhage which means an unnecessary loss of blood to the patient.

As to the method of delivery where forcible dilatation of the os is accomplished, no matter how gently, there will always be cases of postpartum hemorrhage, and I believe that the only cases in which we can be absolutely sure that there will not be postpartum hemorrhage are the ones in which we leave the placental site untouched; that is, cases treated by abdominal cesarean section.

(To be continued.)

NEW YORK OBSTETRICAL SOCIETY

MEETING OF OCTOBER 14, 1930

DR. F. W. RICE reported a case of **Acute Yellow Atrophy of the Liver During Pregnancy with Recovery.**

DRS. E. C. LYON, JR., AND G. G. BEMIS (by invitation) presented a paper entitled **A Study of Neonatal Deaths Occurring in 6000 Consecutive Deliveries.** (For original article see page 373.)

ABSTRACT OF DISCUSSION

DR. WALTER LESTER CARR.—The interwoven character, medical and obstetric, of the report would show the necessity for medical prenatal care being continued during all the time the mother is under observation. There are certain factors which I think we must consider in neonatal deaths, not always detected even though blood and urine examinations are made. For example, a patient contracts influenza just about the time of her confinement and the baby dies of influenza. Such things, I think must be studied in making an analysis of a group of neonatal deaths.

At the Woman's Hospital we examined 200 babies for bleeding and coagulation time to determine whether in babies born with injuries such as cerebral hemorrhage or a tentorial tear, which could not be reached, we could at least inject blood or serum. At present it would appear that we are much better off than when we let those children go without doing anything for them.

Referring to atelectasis and pneumonia, I believe there is no doubt that atelectasis is frequently followed by bronchopneumonia in weak and premature babies.

In the premature and weak groups we must encourage artificial respiration. We cannot, however, always make the baby breathe because the musculature is weak but by proper and not too energetic attention and by the use of oxygen we will be able to get better results.

As for congenital defects, occasionally there is a baby suitable for operation and in one instance of atresia of the duodenum, operation saved the baby, which led us to believe that the way was opened for further operative intervention for this type of defect but the next time a baby had the same symptoms, operation was urged, was not accepted and the child died. The autopsy findings in the latter case showed an atresia too extensive for resection. While there was a mortality of 50 per cent in these two cases, we still felt that the matter of operation in such cases is worthy of attention. Some of the cases of jaundice gave us considerable thought, and various tests have been carried out, and we have felt that these were not always an index of whether the case was a surgical one or not.

Statistical results indicate that greater attention is being paid to newborn babies and while any institution is liable to have an epidemic, such as influenza, this might be avoided or at least minimized by watching the mothers and nurses and at the first sign of influenza having the children isolated and observed for respiratory infection. However, the difficulty is that respiratory infection may be conveyed to a number of babies who show very little rise of temperature for the first day or two and apparently very little change in the upper respiratory tract or naso-

pharynx but because the nasal spaces in babies are so small there is liable to be a quick collapse from descending infection.

DR. LYON (closing).—We have been studying of late the thymus gland in a series of apparently normal babies, having them all x-rayed on the fifth day, to try to determine an index, if possible, for a normal thymus. It is difficult to interpret these x-rays. We have had babies that we felt clinically showed definite symptoms of embarrassment due to an enlargement; these we have treated by x-ray, but in this group in the past eleven years we have not had any cases in which the thymus was the cause of death.

The case of hemorrhage into the adrenals we felt was due probably to handling at the time of delivery. How much spanking that baby had I do not know.

In regard to interpartum and postpartum deaths, our series of stillbirths included the interpartum deaths and the antepartum deaths. I presume that really those two topics should be considered together, the stillbirths and the neonatal deaths, but it makes such a vast amount of figures.

In regard to placenta previa, for somewhat over two years, if I recall correctly, we have been doing cesarean section on every case of placenta previa in which we have made the diagnosis.

We have not had a great many cases, but as yet we have not had any fetal or maternal mortality. Several of these cases have been transfused during the operation, some before, and some afterward. We always have a donor ready and the transfusion apparatus set up, and at times we even have the donor by the side of the patient when we are operating. Lately we have been doing the low flap operation on our cases of placenta previa.

DR. MAX D. MAYER (by invitation) read a paper entitled **Psychotherapy and a Gynecologic Service**. (For original article see page 357.)

DISCUSSION

DR. R. T. FRANK.—Before Dr. Mayer's advent in Mount Sinai Hospital we used a great deal of care in eliminating and weeding out patients whose physical disabilities did not seem to fit the type of symptoms that they complained of, with a fair degree of success, but since he has started this work I feel that these patients are benefited in a further way; not only are we safeguarded from doing unnecessary operative work, but these patients when discharged, are taken care of and again made useful individuals.

DR. J. A. CORSCADEN.—The presentation of such a subject before this group is an extremely healthy symptom of the reaction against over-specialization. It is not so long ago that gynecologic results were expressed in mortality. Even now, discussing the treatment of fibroids, I am frequently told that the best treatment is hysterectomy for any fibroid because the mortality can be brought down below one per cent.

In 1914 I had the privilege of working up a follow-up system which was to cover all cases in the hospital. At that time there was no universal follow-up system that I could find in the country. In a few years after this it became apparent (this was for a surgical service) that the results of surgical treatment were not satisfactory. We at first used vague terms to describe the success of our procedures. We soon had to divide the results into three parts, symptomatic, economic, anatomic. We got beautiful repairs, and beautiful excisions without cure of symptoms, or we might cure symptoms, etc., and leave an economically useless person in the community. My own interest in the subject has come particularly because I have induced in many an artificial menopause. In the early days we

were overwhelmed by the numerous symptoms presented by these sufferers. For years we fed them quantities of ovarian extract but without success. About 1917 in desperation we sought relief from the psychiatric field and found that most psychiatrists regarded these symptoms as primarily psychic in origin and not endocrinologic. So, adopting a crude form of psychotherapy, we have reduced the neuroses to at least a comfortable number.

The problem for the gynecologist is to decide how soon he should turn the case over to a psychic expert.

DR. W. H. CARY.—I think this is one of the major phases of gynecologic practice.

I would like to ask Dr. Mayer whether his work was concerned with a group of outdoor or dispensary patients or with a more intelligent group, because it has been a problem to me to know how to devote the time necessary to properly approach these patients' problems.

DR. MAYER (closing).—With Dr. Corseaden I heartily agree that unless a man has had some special interest or training in the subject he is apt to err in the direction of giving advice. The essential feature for us, as gynecologists, is to be able to see that there is a disproportion between the effects and causes and look for a residual phenomenon.

In answer to Dr. Cary I would like to say that this report is based solely upon cases seen in the hospital and the out-patient department, where the work was done for seven years before its being included in the ward. My private experience has not been included in this paper.

I have devoted some time, but I find that the time necessary is not excessive. The special morning clinic has an attendance of less than a dozen cases on the average and outside the regular round hours and in spare hours during the day the cases in the ward are interviewed. I have three assistants who are being trained in the out-patient department to collaborate in this work.

THE OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF MAY 1, 1930

DR. CHAS. C. NORRIS, the retiring President presented an address, after which DR. JOSEPH V. MISSETT described **A Case of Primary Tuberculosis of the Cervix.**

Mrs. F. S., aged fifty-seven years, white, a native of Philadelphia, nullipara, was admitted to the Women's Neurological Department of the Philadelphia Hospital in January, 1930, for the treatment of a left hemiplegia suffered a week before. Other than the paralysis, her complaints were: gnawing pain in the left hip, lower abdominal and lumbar pain of one month's duration, pain in the left shoulder girdle, and vaginal discharge for two months.

She was quite certain of the duration of the discharge, dating its onset following a physical strain. "Felt something rupture after I lifted some tubs, and then the flow began" is her statement. Her family doctor told her her womb was twisted and prescribed a douche, which brought no relief. She was a robust, healthy looking woman, well preserved and whose weight had been well maintained. However, she was extremely neurotic and apprehensive, and examination was rather difficult because she was in fear of being hurt.



Fig. 1.—Cervix and anterior vaginal mucosa, showing excavating ulceration above anterior lip of cervix, with an area of subepithelial injection to the right of the ulceration. The cervix is atrophic.

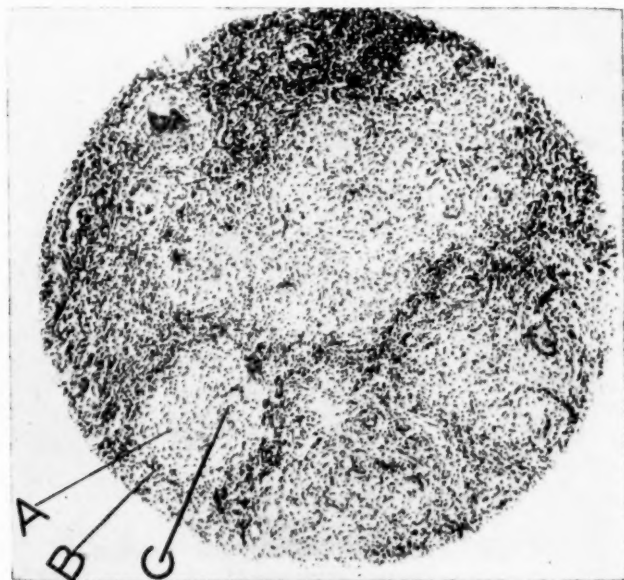


Fig. 2.—Photomicrograph, low power, showing individual and conglomerate tubercle formation. *A* Represents the center of a tubercle, *B* the zones of epithelioid and lymphoid cells surrounding the tubercle *C* a typical Langhans giant cell.

Her past medical history was essentially negative. Her family history was negative, except that her mother died at the age of sixty-three, supposedly of carcinoma of the liver. The patient was married at the age of twenty-four, her marital relations were presumably normal, and her husband was a hard working individual weighing well over 200 pounds. She denied intercourse out of wedlock.

Her menstrual history is unusual. At the time of admission she claimed that at the age of eighteen she had three menstrual periods, spaced at regular intervals of twenty-eight days, with scanty flow for two days and profound dysmenorrhea. There was then a cessation until the age of thirty-eight. Subsequently the patient denied menstruating at the age of eighteen, and stated she menstruated for the first time at the age of thirty-eight. At that age her periods were regular for nine months, menstruating only for a day, however, and with scanty flow; following this she complained of headaches, hot and cold flushes for a long period of time, and profound nervousness.

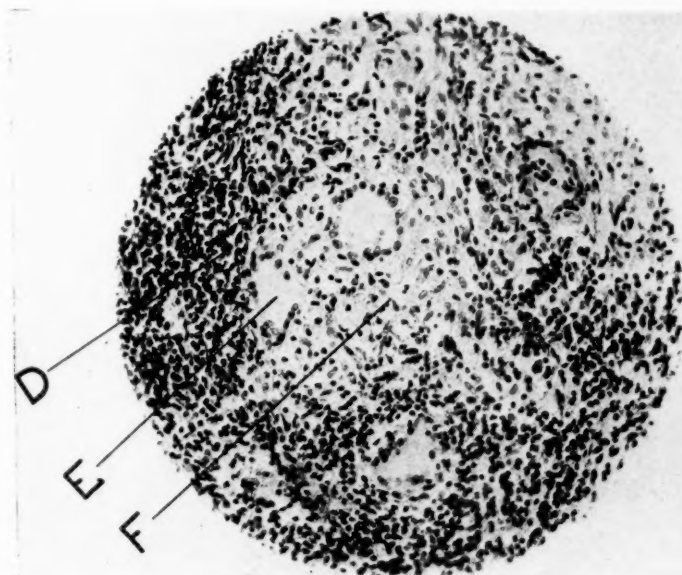


Fig. 3.—Photomicrograph, high power, of tuberculosis nodule in tissue removed for biopsy. *D* Indicates the ring of epithelioid and lymphoid tissue surrounding the tubercle, *E* a typical Langhans giant cell with its peripherally placed nuclei, *F* central area of tubercle showing little caseation.

There was no evidence of bone or joint disease, the hip, lumbar area, and left shoulder girdle being ruled out by physical examination and x-ray. Lungs were clear and the x-ray of the chest was negative. There was tenderness throughout the whole abdomen, but it was more apparent than real. The patient could be made to relax and the abdomen could be palpated quite freely. No masses were felt.

A foul smelling, grayish-yellow, purulent, necrotic vaginal discharge was noted. The vaginal mucosa was atrophic or senile. Cervix small, irregular and indurated. Uterus senile or atrophic. No pelvic masses. Unable to feel adnexal abnormality. The tubes and ovaries were considered to be also atrophic. By speculum examination, the cervix was found to be small, with a small closed os. Fairly normal posterior lip. The anterior lip showed what appeared to be an ordinary erosion with excavating ulceration that bled only slightly on vigorous rubbing. Above the actual ulceration was an area of subepithelial injection on the vaginal portion

of the anterior cervix representing an inflammatory extension. The consistency of the cervix was firm. No cysts or granular areas. There was bleeding from the cervix after trauma.

Biopsy report on cervical tissue was as follows: Section shows numerous epithelioid tubercles in which there were many typical Langhans giant cells. There was little caseation. There was no evidence of malignancy.

Diagnosis.—Tuberculosis of cervix.

A second biopsy specimen was taken about two months later and was reported upon as follows: The tuberculous nature of the lesion was not so well demonstrated by this biopsy as by the former. However, the combined picture presented by the sections was entirely convincing.

The further clinical course was, for the most part, an afebrile one. Blood pressure 145/90. Urine examination showed a high specific gravity, trace of albumin and many leucocytes. Blood count was as follows: Hb 12.3 gm., W.B.C. 7000, R.B.C. 4,130,000 and a normal differential count. Blood chemistry was normal. Three special urine examinations revealed no tubercle bacilli.

Comment.—At the present time a final diagnosis of primary tuberculosis of the cervix in this case cannot be made with absolute accuracy. The patient would not submit to surgery as a curative measure, and our diagnosis therefore is based on the physical findings, the microscopic examination of tissue removed from the cervix for biopsy, the absence of associated pelvic pathology, and our failure to discover foci in other parts of the body.

The clinical picture was not wholly unlike that of early carcinoma of the cervix. In fact the tentative diagnosis, before the biopsy findings were reported, was early malignancy. This feature in the case is important, in that it lends further emphasis to the need for microscopic examination of all tissue held pathologically suspicious.

DR. LEONARD C. HAMBLOCK reported and described **Two Cases of Acute Puerperal Uterine Inversion.**

CASE 1.—M. S., primipara, aged twenty-one. The prenatal blood pressure ranged from 90/75 to 100/75. Her only complaint during this time was fatigue. Entered hospital May 20, 1929 with pains every ten to twenty minutes. Membranes unruptured. Rectal examination showed head in pelvis, cervix not entirely effaced, one finger dilatation. Pains not very severe until 6 A.M., when they became more severe and regular at two to three minutes. Cervix three fingers' dilatation and fully effaced. At 10 A.M. she was taken to delivery room with fetal head on perineum. Gas anesthesia begun, membranes ruptured, outlet forceps applied. Episiotomy done and the baby delivered without difficulty. Sutures were placed in perineum, but not tied, no excessive bleeding. When anesthetist stated the pulse at 140, the clinic nurse could not feel the fundus and placenta was presenting itself at the vulva. Anesthesia was stopped and an attempt was made to deliver the placenta. As it was brought through the vulva it was firmly adherent to a pale pear-shaped object, the uterus. Intravenous injection of salt solution begun and while this was running in, the placenta was separated manually and pressure made on the outer margins of the inverted uterus to replace it. The hand followed the fundus as it quickly righted itself, packing was immediately placed in the uterus, heat applied to the body, feet elevated and the pulse watched carefully. Salt solution, 300 c.c., given and the pulse gradually settled down to 110. One hour later patient was put back to bed. Digalen administered hypodermically. In the early evening pulse was 90, and the next morning the packing was removed and sutures in the perineum tied. She made an afebrile convalescence, nursed her baby and was discharged on the fourteenth day.

Examination of this patient on July 26, 1929 showed a well healed perineum, slight unilateral laceration of the cervix, uterus in good position adnexa negative and no tendency to prolapse.

CASE 2.—E. P., primipara, aged forty-one. Prenatal blood pressure varied from 128/90 to 140/80, when she began to complain of slight edema of hands and ankles. Urine at this time showed cloud of albumin and a few hyaline casts. Next examination showed blood pressure of 165/90 with an increase of edema of feet and hands. Since this was definitely a case of toxemia she was admitted to the hospital for induction of labor three weeks before term. Castor oil and quinine were given without results and a surgical induction was done. A Voorhees bag was inserted at 12:10 P.M., March 28, 1930. For two hours no pains and a pound weight was attached to the bag. This caused irregular pains and at 12 midnight the bag had slipped through the cervix. Rectal examination showed a well effaced cervix, no engagement of the head and the cervix dilated three fingers. She was taken to the delivery room, ether anesthesia given, cervix dilated easily manually and version performed. There was no difficulty, forceps were applied on the after-coming head, no suprapubic pressure made, episiotomy was done. Almost as soon as the cord was cut, the placenta was at the vulvae and the patient's pulse had risen to 156. Placenta was delivered with the inverted uterus attached, the placenta separated manually, uterus replaced and packed, hypodermic of 30 c.c. of Digalen given. Since this patient did not present the evident shock as the first patient had done, no further treatment was given. Pulse dropped to 140 and she was transferred to bed. The next morning pulse was 120, temperature 100.2°, blood pressure 120/80. Packing was removed, the patient remained afebrile. Episiotomy was required on seventh day, and the patient left the hospital on the seventeenth day. Examination April 26, 1930 showed a well healed episiotomy, small bilateral laceration of the cervix, uterus well involuted and in good condition. Blood pressure 130/90. Urine, trace of albumin, no casts.

In reviewing our two cases the following interesting points may be noted:

1. The two extremes of childbearing age are represented.
2. The lesser shock in the second patient, due no doubt to the earlier recognition of the condition.
3. Rapid recovering from shock in both cases.
4. Ease of reposition by taxis.
5. Absence of sepsis.
6. Absence of excessive hemorrhage.
7. The first case presented a hypotension during her prenatal term, the second case showed toxemia with hypertension.
8. Inversion followed after two widely different methods of delivery.

DISCUSSION

DR. PHILIP F. WILLIAM.—Although the condition is quite rare I have seen three cases myself. In the first, the woman had been delivered by forceps, sutures had been placed in the perineum but not tied, placenta was manually extracted when the fundus turned inside out. The shock was severe, so the vagina was packed and she was sent to the hospital. I saw her on her arrival, treated her for shock, the examination showed that it was impossible to reduce the inverted fundus by taxis because the cervix was so tightly contracted. She died within an hour after admission.

In the second case, I saw the patient, a primiparous woman, five years ago following a forceps operation. The doctor had done a manual removal of the placenta, which was followed by inversion. There was great hemorrhage and shock. She

was sent to the hospital, given morphia and saline and seemed to rally, and it was decided to attempt reduction by taxis, but this failed and the patient died on the table.

These cases showed what an enormous degree of shock patients suffer after inversion of the uterus.

In the third case I saw the patient only two years ago. It was a primiparous labor delivered by forceps. The placenta was expressed by Credé and immediately the presence of a tumor mass was noted in the vagina, and as this patient was still under the anesthetic, reposition was immediately done, she was packed, had very little shock, and recovered.

I believe it is still true that almost every case of inversion of the uterus is due to some mishandling of the third stage of labor. I heard of one case a few years ago where the placenta remained attached, and the uterus spontaneously inverted following the use of two doses of 1 c.c. each of pituitrin. Since then I have almost invariably had pituitrin given after the completion of the third stage for fear some accident might be caused by over-stimulation in cases where the placenta is still attached.

I think that probably where less haste is made in the third stage of labor less harmful results ensue.

DR. WILLIAM R. NICHOLSON.—I witnessed a case of this kind some years ago, following a careful delivery by forceps. There was no attempt at the Credé method because of lack of time. Inversion of the uterus occurred immediately after delivery. The placenta was removed immediately, reposition done manually, and the patient did well.

Another case was of a woman with a two-thirds inversion, the particular point about this case being while the inversion had been in evidence for some two and a half hours before I saw her, there was no shock and but relatively slight hemorrhage. I told the anesthetist to put the patient under the surgical degree of anesthesia and then simply replaced the uterus by pressure.

I believe deep anesthesia was the important factor in my success in this instance.

In these cases I believe that there must always be a degenerative muscular change in the uterine wall, analagous to what probably occurs in premature placental separation, which permits invagination of a portion of the uterine wall. This invaginated segment then becomes as it were a foreign body in the uterus and under the action of the uterine muscular contractions is progressively pushed out.

With regard to the etiology of inversion, I am perfectly certain that the Credé method has very little, if anything, to do with it; and while of course I do not advocate traction on the cord, I feel that this also has very little to do with it. In other words, as I believe that premature separation of the placenta predicates some disease of the uterine musculature, so do I also believe that the same predisposing factor is operative in cases of inversion. In the two instances of this latter condition which I have seen there was no question of cord traction or forcible manipulation of the uterus in either.

I cannot agree with Dr. Hamblock on the question of pituitrin. Its dangers are the same as that of any powerful drug, if given in an overdose, but as far as these cases are concerned, I am perfectly certain that a dose of pituitrin following the delivery of the baby works against the probability of inversion rather than for it.

One more point I would like to make is that it seems to me that in cases occurring outside hospitals where the possibilities of clean, rapid work are out of the question, that the placenta in cases of inversion had better be left alone, until transfer to hospital can be made. Pack the vagina if necessary because of hemor-

rhage, but as a general rule the immediate removal of the woman to the hospital, with the placenta attached, gives her a better chance than an attempt at reposition in the house.

DR. GEORGE M. BOYD.—The cases I have had of acute inversion of the uterus bear out the viewpoint expressed, namely: the uterus is at fault, for many of these cases are spontaneous. The acute cases have yielded to taxis but I have found it necessary to operate in two. The first was one of complete inversion and failure to reposit the uterus by taxis, it was necessary to do an abdominal section for the purpose of making manual dilatation of the cervix. The second case was one in which the uterus had been inverted for sixteen months. An anterior colpohysterotomy (the Spinelli) was performed with success and it is interesting to know that this woman has had two babies since the operation.

In the treatment of so rare an accident, few have had an extensive experience. This fact probably explains the general hesitancy in the past to accept early operative measures. The operator has often persisted in taxis or the use of some mechanical device or pessary to the detriment of the patient. On the other hand, some operators failing in taxis, recommend hysterectomy for all chronic cases. This operation is indicated where there exists gangrene or marked infection of a tumor of the uterus but in clean cases, it is unjustifiable. In the acute case before involution is completed the uterine musculature is still hypertrophied. It is pliable and will often yield to taxis. Manual reposition should therefore be tried in all such cases but after a month or six weeks the uterus will have returned to its normal size and the tissue become firm and unyielding. In these chronic cases, manual reposition should only be carried out for a short time, if at all. By early operative measures, mortality and the comfort of the patient will be materially improved. Colpohysterotomy is therefore the operation of choice in the treatment of difficult cases. It is conservative, simple of execution and can practically be applied to all. Should the anterior operation fail, the posterior wall of the uterus could also be incised. This would undoubtedly make it possible to reposit the uterus. Anterior colpohysterotomy, the Spinelli operation, has certain advantages over the posterior. The field for operation is more accessible and suturing is facilitated.

DR. GEORGE W. OUTERBRIDGE.—I saw in consultation about a month ago a young primipara, with a complete inversion of the uterus, who had been delivered about five hours before. I believe the placenta had remained attached for about an hour, at the end of which time it was expelled without difficulty by the Credé method. The patient, however, continued to bleed and went into shock. The attending physician made a tentative diagnosis of inversion of the uterus and attempted to replace it but was unsuccessful. The vagina was then packed as firmly as possible around the inverted uterus. When I saw the patient she was in extreme shock and almost completely exsanguinated. Blood was being taken from her husband for a transfusion, and in view of the intense shock, I felt it better to wait until after this had been given before attempting to do anything. The patient received about 450 c.c. of blood. By this time the vaginal packing showed oozing through it, and the patient's condition was slightly, if any, improved. It did not seem justifiable therefore to procrastinate any longer, and I removed the packing and without anesthesia was able comparatively easily, by making pressure on the center of the inversion, to replace it completely. The uterus was then firmly packed, but the patient was in a desperate condition. A second donor was on hand, and blood was obtained from him for a second transfusion, but the patient died before it could be given. I felt that this patient's life could probably have been saved had it been possible to replace the uterine inversion and pack the uterine cavity before so complete exsanguination had taken place. The only possible predisposing condition in this case that I know of, which may or may

not have had any effect, was that about a year previously she had had an incomplete abortion, for which an ordinary dilatation and evacuation of the uterus had been done.

DR. W. E. PARKE.—It is my practice at the Kensington Hospital for women to administer an ampoule of pituitrin as soon as the baby is delivered, and in several thousand cases, no untoward accident has occurred. I believe this practice would oppose rather than favor inversion of the uterus.

DR. P. B. BLAND, DR. L. GOLDSTEIN, AND DR. D. H. WENRICH presented a paper entitled **Trichomonas Vaginalis Vaginitis in Pregnancy**. (For original article see page 365.)

DISCUSSION

DR. P. BROOKE BLAND.—Nearly one hundred years ago (1836) Donne referred to the trichomonas as the possible provocative factor in cases of persistent leucorrhea. Since then more than 60 papers, have appeared, both in this country and in Europe, supporting this view.

In order to determine the causative relationship of the parasite to obstinate leucorrhea and especially its possible influence on the normal vaginal flora, and thereby its ultimate relationship to puerperal morbidity, we have systematically examined the vaginal secretion of all patients registering in our Antenatal Clinic.

We have not carried our investigations far enough to express an authoritative opinion with reference to the rôle the parasite may play in puerperal morbidity, but we do believe that it does give rise in some patients, though by no means in all, in whom it is found, to a definite pathologic entity, characterized by minute pinpoint areas of hyperemia and granulation in the cervix and vaginal walls, especially in and about the vault, accompanied by a profuse bubbly discharge.

For a time, I must confess, I was somewhat skeptical as to whether the organism was capable of bringing about pathologic tissue alteration, but substantial proof of its pathogenicity seemingly is found: First, in the numerous papers published dealing with this phase of the problem. Second, because of the fact that it is transmitted from one individual to another; and, third, by the rather characteristic tissue changes which take place in individuals to whom it is transferred.

DR. WILLIAM R. NICHOLSON.—I should like to know whether any pathologic symptoms have ever been found in the mouth as a result of infection with this organism. I should also like to know about the permanence of the suggested culture media, because it would be extremely difficult to carry out this work in a clinic if the culture media was not of a lasting quality. I still doubt whether there is any relationship between this organism and puerperal morbidity.

DR. LEOPOLD GOLDSTEIN.—The organisms are very easily found in the fresh smears of vaginal secretion. They will remain alive for a number of hours or even overnight in an ordinary saline solution; but a little difficulty is encountered in cultivating them.

We are trying to determine the source of these organisms. Later we shall examine the mouths of these patients in order to determine whether there is any relation between the organism found in the mouth and that found in the vagina. As far as its effect on morbidity is concerned, a number of European writers have found that there is a definite relationship between trichomonas infection during pregnancy and morbidity after delivery.

THE OBSTETRICAL SOCIETY OF PHILADELPHIA

STATED MEETING, OCTOBER 2, 1930

Report of the Committee on Pregnancy Toxemia, presented by DR. EDWARD A. SCHUMANN. (See page 381.)

ABSTRACT OF DISCUSSION

DR. J. O. ARNOLD.—One of the first points in the study and care of toxemia is to properly classify women in pregnancy with reference to the status of the kidney condition. I have felt, from my own observations, for some years, that there is a definite toxemia of pregnancy, which affects women according to whether they have *now*, or have *had*, any kidney disease; or whether they are *now*, and always have been, *free* from kidney disease. If we can make that classification from the start, we will have done a great service toward the treatment, or prevention of toxemia.

We must, therefore, have more thorough and efficient methods of study of kidney conditions at the very beginning of pregnancy. Those cases that show any indication (for instance, by eye, or other examinations) of previous kidney disease, are treated in an entirely different manner from those which are known to be kidney-free at the beginning of pregnancy.

As to the direct treatment of the eclamptics or preeclamptics, it seems to me that one of the greatest advancements that have been recorded recently is that of more careful attention to the "fluid balance," as suggested by the work of Temple Fay.

I agree that most of these patients require very little of the more or less radical treatment we have been giving them. Very few will require morphia. Blood-letting, I think, or spinal drainage, will continue for some time, and in some instances magnesium sulphate, or perhaps better, 50 per cent glucose injected intravenously may have beneficial effect. But for most cases very careful attention to the relationship of intake and output of fluids, and to methods of fluid elimination—keeping the intake *always* several ounces below the output—will undoubtedly prove a most important factor in successful treatment.

DR. JOHN M. LAFFERTY.—The trend of all recent work on eclampsia has tended to show that the cause of this disease will ultimately be found to be due to some disturbance of the maternal metabolism, instigated by the growing fetus. A study of the blood chemistry especially in relation to the various metabolic constituents, will therefore be the key by which this problem will be solved. The work of a number of investigators, especially the pioneer work of Titus, has demonstrated the fact that the carbohydrate metabolism is especially important, as the fetus is nourished largely by this element in the mother's blood. One man has the opportunity of seeing comparatively few cases of this disease, and hence a careful study of the blood chemistry of all cases of eclampsia seen by men who have the facilities of a laboratory would supply data of considerable value in clearing up the cause.

I have had the opportunity of collecting blood for examination from six patients in eclampsia, the results of which I am preparing to report at a later date. They all show, I think, a significant fluctuation when taken at five-minute intervals as advised by Titus, and most of them show relatively low average

values. The blood was examined by the method of Folin and Wu which gives a normal variation in blood sugar for 80 to 120 mg.

In all cases there was found a drop of blood sugar preceding the convulsion, followed by a rise after the convulsion.

If this fact is considered in the light of the investigation of the Cori brothers who found that the secretion of the adrenals in a deficiency of oxygen caused the glycogen in the muscles to be incompletely oxidized into lactic acid, which in turn was reconverted into glucose by the liver, it would seem that the convulsions of eclampsia were a protective mechanism of the body to maintain the blood-sugar level. The destructive nature of the convulsion does not mitigate against this view, as other protection reactions, e.g., fever, can be so exaggerated as to destroy instead of conserve.

DR. J. STUART LAWRENCE.—I would like to discuss three aspects of this report.

I. The Method of Investigation.—To establish even a method of investigating the problem of toxemia is difficult. Perhaps another method than that adopted by the Committee might be more successful. In my opinion a better method of procedure would be to have one man from each hospital service, designated by the chief of service, to prepare and report the toxic cases and their incidence according to their own hospital's methods. Each of these men would collect, classify, and analyze their own data from the standpoints of incidence, etiology, classification, and treatment; each of these men to be members of the Committee, together with other men chosen for their special interest in toxemia and especially research workers. Then at the end of a given period and during the period the Committee so composed should be divided into subcommittees by the chairman to collate and analyze and report on the material, methods, and status of the toxic problem. Such a method would perhaps give us a better statement of each hospital's ideas, method, and experience, which would really be the starting point of an investigation.

II. Treatment of Eclampsia.—In order to put myself on record, I wish to say that I employ the conservative method, that is, the Rotunda supplemented by the Titus method.

III. Avoidance of Toxemia.—I believe that the treatment of actual eclampsia cannot go much farther than it has. You will have noticed that one-half of the patients in eclampsia here reported had received prenatal care. Therefore, in the future our course should be to put more and more emphasis on the avoidance of such a result. But toxemia cannot be avoided more thoroughly unless the prenatal clinics become more efficient, and unless toxemia is recognized early. In my opinion this cannot be accomplished if dependence is placed solely on a rise in blood pressure to always give the earliest warning. Although it may be an heretical statement to make, I wish to say that in St. Mary's clinic blood pressures are not determined at all, because it is believed that other ways exist—means of which warning of the approach of toxemia is more certainly and more frequently given. I would illustrate these means by briefly analyzing our experience for the first half of 1928, one of the years embraced in this survey. In the first six months of 1928, the material in the clinic of St. Mary's consisted of 112 cases, which classified by our method consisted of nontoxic 49 cases, mild stage 28 cases, severe stage 35 cases, eclampsia no cases.

DR. THADDEUS L. MONTGOMERY.—From my experiences with toxemia as we meet it among the patients in the Dispensary, I am quite convinced that blood pressure reading and urinary findings do not always forecast some of the most serious cases. In many of the latter, the patient's symptoms and her appearance

upon examination is a truer guide of a state of her health than of the developing toxemia. I think we must devote more attention to studies of liver function in these patients. By so doing we will find more definite signs of approaching toxemia than are indicated in the urine or blood pressure.

DR. PHILIP F. WILLIAMS.—My hope that something in the nature of what we have heard this evening might result from the forming of the Committee has been fully justified. It is disappointing to hear of these cases of women reported as dying of toxemia of pregnancy during the two years quoted; and yet how few have been brought to the attention of the Committee.

I regret that one of my services includes one of the cases that was mentioned. This woman's death brings up a sidelight on some of the deaths which occur in convulsive toxemias of pregnancy. This woman had had no prenatal care, was a multipara, thirty-eight years old, and came in with convulsive toxemia. We were able to quiet her with a modified Stroganoff method. She was spontaneously delivered. Her condition, however, did not improve; temperature became high, and after four or five days she died. We hardly felt she had puerperal sepsis, and insisted on an autopsy, which was granted. It was found that the woman had very severe ulcerative colitis. From these ulcers in the colon, ascending transverse and descending colon, streptococci were recovered similar to those recovered from her urine. They were not recovered from blood cultures which were taken.

In the women whose cases we might call low reserve kidney toxemia, or nephritic toxemia, rather than preeclampsia, we have used the technic recommended by Lazard of Los Angeles, using injections of magnesium sulphate intravenously. I am convinced, however, that in a large number of cases as good results can be obtained from rest in bed and from low protein diet. Where the case does not improve, we have speedily resorted to surgical induction of labor.

In two cases which came in my services during the time of this report, I did cesarean section. Both of them were done under a local anesthetic, both recovered, and both babies did well. I am certainly convinced that a mild narcosis and a local anesthetic give a very favorable opportunity for speedily terminating pregnancy where toxemia is present. I have used it on account of the work which Stander has brought out, showing that any type of inhalation anesthesia serves to promote or increase acidosis.

American Journal of Obstetrics and Gynecology

GEORGE W. KOSMAK, M.D., EDITOR

HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

Editorial Comments

The White House Conference*

THE medical service of this important gathering for the study of Child Health and Protection has just held its concluding session in Washington.

The present Conference was called and sponsored by President Hoover, who is deeply interested in child welfare. The Honorable Ray Lyman Wilbur, M.D., Secretary of the Interior, acted as Chairman. The first child welfare conference sponsored by a President was held during the administration of Theodore Roosevelt and another during Woodrow Wilson's administration. Neither of these was in any sense as elaborately planned and carried out as the last, which is the most comprehensive of all.

The purposes of this gathering were to study the present status of the health and well-being of the children of the United States; to report on what is being done for child health and protection; and to recommend what further ought to be done and how to do it.

The comprehensive character of the movement is evident from the direction that it should consider the child from its conception to the eighteenth year of life. Naturally, it would have been undesirable to exclude the mother from consideration, but an attempt was made to regard her welfare only in so far as it affected the fetus, infant, and child.

To the physicians of the country the labors of the Conference are of the greatest interest and importance and a study of the findings of the various Committees when these are published should be carefully read and pondered by everyone engaged in obstetric work.

The Committee on Prenatal and Maternal Care was divided into several subcommittees which studied various aspects of maternal care

*A later issue of the JOURNAL will be devoted to the publication of the principal reports presented to the Conference.

in its relation to child health and protection. The statistics of maternal mortality in the United States are not encouraging, and together with fetal and early infant mortality they show little or no decrease in recent years. It is probable that more complete and accurate returns and a better classification of the causes would be of help in determining what should be done in the possible prevention of these deaths.

The Conference brings out again the fact that we have annually in the United States approximately 15,000 maternal deaths, 80,000 deaths of infants under one month and 85,000 stillbirths. It matters little what relative position the United States occupies in the list of civilized countries. The important facts are that we are not improving our rates and that most of these deaths occur from controllable causes. The recent study of the Children's Bureau carried out with the co-operation of State Boards of Health and Medical Societies shows that 40 per cent of the maternal deaths result from sepsis, 26 per cent from toxemia and 11 per cent from hemorrhage. A great majority of these women never had proper prenatal care; inductions of labor were frequent and many had operative deliveries. Live births resulted in only 42 per cent. These studies likewise show that abortions and premature labors were frequent; about 50 per cent of the septic deaths followed termination of pregnancy prior to the seventh month and naturally all of these fetuses died. The stillbirth rate has not changed materially for years and the early infant death rate remains unaltered year after year, while the activity of the pediatricians in stimulating infant welfare work and improving the practice of pediatrics has resulted in a reduction of the later infant death rate. The chief causes of these early infant deaths are prematurity, birth injury, congenital malformations, and infections, including syphilis.

The obstetricians must accept the challenge to correct these conditions. As an individual one can do little, but collectively much could be accomplished. The reports of the committee on Prenatal and Maternal Care brought out much of importance and among other things the shortcomings of education and training in obstetrics were stressed. The training of the undergraduate student in clinical obstetrics was found to be inadequate in many schools. Most schools and states do not require an intern year as a requisite for graduation and the granting of a license to practice obstetrics. The opportunities for the further training of graduates are very meager. Something has been accomplished for the general practitioners by means of the extension and circuit courses which have been given in some of the states. The facilities for the training and teaching of specialists to practice and for positions as teachers and investigators

have been insufficient to meet the needs of the country. There has been gradual improvement in the past few decades, but there is still much to be desired.

The midwives, whose mortality results are in general not higher than those of doctors, have had little opportunity for satisfactory training. It is necessary that they should have facilities for such education if they are to continue in this work. They are needed among the negroes and in certain localities which are sparsely settled, but they should carry on their work under medical supervision and control.

The training of nurses in maternal care has been insufficient and steps must be taken to improve it. The working out of maternal welfare in various communities by a combination of nurse and doctor offers splendid opportunities for success in giving better care to mothers and babies.

In order to secure the best results, it is necessary to have the laity educated to seek and demand adequate attention. The social workers should also be fitted into the scheme and can give valuable aid in helping to solve many family and economic problems related to maternal care.

It is vitally essential in order to secure the necessary results that plans and organizations be developed in each community to furnish every mother competent and consecutive prenatal, intranatal, and postnatal care. The doctors should and must lead in their own communities to secure "for every child full preparation for his birth, his mother receiving prenatal, natal, and postnatal care; and the establishment of such protective measures as will make childbearing safer."

—*Fred L. Adair.*

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

Selected Abstracts

The Pathologic Puerperium

Young, James: Maternal Mortality from Puerperal Sepsis. British Med. J. No. 3518, p. 967, 1928.

According to the official figures for 1926 the total maternal mortality for England and Wales was 5.14, and the sepsis mortality 1.60, per 1,000 live births.

Septic inflammation of the genital canal during labor or in the puerperium may, as a useful basis for analysis, be considered as falling into one or other of three clinical types according as it is caused by (1) contagion, (2) trauma, or (3) auto-infection.

Autogenous infection is a minor primary cause of fatal puerperal sepsis.

Contagion is probably of comparatively secondary importance. The well established risks of contact infection in hospitals call for care in the extension of the hospital system of maternity service.

There is evidence that trauma is the most important cause of the death rate from sepsis. This is not entirely a problem involving the medical attendant; it has implications of a wider nature.

The immediate need is an improved machinery for maternity practice based on a midwife-doctor combination. From the standpoint of immediate policy the importance of this overshadows all other considerations, for example, "research" and there is reason for the hope that by this means alone a lessening of the death rate is possible.

Improved education of the public, the midwife, and the student, and the assistance of the central and local authority, are all necessary for the creation and working of a satisfactory machine.

PROSHEK.

Hobbs, A. Remington: Puerperal Sepsis. British Med. J. No. 3518, p. 971, 1928.

Conclusions arrived at as the result of the research work carried out at St. Mary Abbots Hospital during the past few years are:

Puerperal sepsis is not by any means invariably accompanied by a rise of temperature. Pyrexia is merely a sign in the course of a septic process, and this is one of the main reasons why a large number of cases of puerperal sepsis are allowed to pass unrecognized through our best maternity hospitals.

Inflammation can be caused by agents other than bacteria. Retained blood and fragments of membranes or placenta will act as foreign bodies and will lead to inflammatory changes in the uterus.

Pain and tenderness must be recognized as the commencement of uterine colic and obstruction. So long as the symptoms and signs of acute uterine colic and obstruction are not added to the list of abdominal inflammations, and are not

treated as soon as they appear, so long will patients be subjected to abdominal explorations, whereas they might have been saved.

It will soon be no longer the fashion for women to bleed for weeks, months, or even years after their confinements, because students will be taught that glycerin will relieve the inflammation which produces the hemorrhage. The best time for treatment is in the early days of the puerperium.

After curetting and swabbing with strong styptics, the uterus must be drained for the succeeding few days.

PROSHEK.

Eden, T. Watts: National Inquiry into the Causes of High Maternal Mortality Rate. British Med. J. No. 3576, 81, 1929.

The National Committee, set up by the Ministry of Health to investigate the causes of maternal mortality in England and Wales, will not be in a position to report for some time, but a similar investigation in the city of Aberdeen, made for the last ten years, has just been completed.

It deals with the following factors influencing maternal mortality; general health of the mother, her surroundings, antenatal supervision, toxemias, hemorrhage, hospital vs. home care, doctor vs. midwife, and puerperal sepsis.

1. General Health. The maternal death rate among unmarried mothers is double the total rate, and mortality from sepsis is presumably much greater than in her married sister. Classifying health as "good," and "unsatisfactory" only 40 per cent of all the mothers who died were classed as having good health.

2. Housing conditions such as overcrowding and deficient cleanliness have no apparent influence in increasing the risks of childbirth. The same may be said of stringency of means.

3. Antenatal Supervision. The death rate among those who received antenatal care was only half the rate among those who did not.

4. Toxemias. Institutional death rate from albuminuria and convulsions among patients over whom these institutions had full control throughout pregnancy was two and a half times as high as the general rate for that condition for the city, the rates being 2.7 and 1.0 per thousand respectively.

5. Hemorrhage. No distinction is made between antepartum and postpartum hemorrhage. Institutional death rate from this cause excluding emergency cases is double the general rate, 1.4 and 0.7 per thousand respectively.

6. The total maternity death rate for the city from all causes over the ten year period was 6.6 per thousand. Death rate in institutions among patients whom they supervised throughout pregnancy, was 14.9 per thousand. The corresponding rate for those attended by private doctors was 6.9 per thousand, by midwives only 2.8 per thousand, by midwives with medical assistance 2.5 per thousand, and by hospital assistants in the district 5.6 per thousand.

7. Sepsis. The general rate for Aberdeen was 1.5 per thousand, about the average for the whole country; the institutional rate, excluding emergency cases, was 4.5 per thousand, in hospital districts only 0.7 per thousand, and among the practice of doctors and midwives well below the average.

A hemolytic streptococcus is the causative organism in all but a small minority of cases. Its natural habitat is the throat. The theory is that this organism is borne from carriers by droplet infection, directly or indirectly, to the genital canal. The possibility that streptococci may make their habitat in the cervical and vaginal secretions during pregnancy, and may become active after labor and invade lacerations or placental site, while admitted, is believed to occur in only a small proportion

of cases. The reason for a higher death rate among cases delivered by doctors than among those delivered by midwives is that doctors are brought more frequently in contact with other diseases of streptococcal origin and are thus more likely to become carriers. The droplet infection theory as the main etiologic factor is by no means proved, and should conclusive evidence in favor of it be adduced in the future, the problem of what to do with these carriers will be an enormous one, as probably the majority of healthy persons are throat carriers of the hemolytic streptococcus, and no mask worn by medical or nursing attendants absolutely prevents droplet distribution.

A striking fact is that in this city most of the deaths from sepsis occurred during epidemics. A single case of acute infection may occur and be spread by gross contagion from one woman to another and also to the infants. This being so, all maternity hospitals should be provided with *isolation blocks* to which all infected cases should be sent as soon as infection becomes manifest, and when feasible an intensive study should be made of those cases by a combined team of obstetricians, bacteriologists and public health authorities.

GEORGE E. HUDSON.

Peterson, L. S.: Causes of Death in the Puerperium. Acta obst. et gynec. Scandinav. 9: 432, 1930.

Among 24,155 labors there were 165 maternal deaths, or 0.7 per cent. In about 50 per cent of the cases, death was due to infection or toxemia, these two causes being responsible for an almost equal number. Placenta previa was the cause of death in 10 per cent. In many cases of toxemia and placenta previa, death was caused by infection, hence the latter was ultimately responsible for about 40 per cent of all the cases. Five deaths were due to rupture of the uterus and 4 to postpartum hemorrhage. Of the causes not directly associated with pregnancy, pneumonia during the years 1918-20 had a very high incidence. Renal and cardiac disease likewise had a high mortality but very few women with tuberculosis died in the obstetric clinic.

J. P. GREENHILL.

Jeannin C., and Sureau M.: Statistics of Puerperal Infection. Bull. Soc. d'obst. et de gynéc. 18: 192, 1929.

The authors review a large series of cases treated in various ways. They divide their statistics into several parts, the first of which deals with the general statistics of 12,500 labors. In the second part they analyze the cases received from different sources in an isolation service. They found that among every 1,000 women who give birth, 25 develop puerperal infection. In every 1,000 cases 6 women die, two of whom die of puerperal sepsis. In each 1,000 labor cases there are two cases of periuterine infection, two cases of phlegmasia alba dolens, one of peritonitis and one of septicemia. In each 100 cases of puerperal infection there are 7 cases of periuterine infection, 3 cases of suppurative pelvic phlebitis, 5 cases of peritonitis and 5 cases of septicemia. Out of every 100 deaths from puerperal infection, 5 are due to periuterine infection, 22 to suppurative phlebitis, 38 to peritonitis, 33 to septicemia and 2 to other causes such as embolism and uterine gangrene. The mortality for women with periuterine infection is about 8 per cent, for those with suppurative uteropelvic phlebitis it is 100 per cent for the cases not operated upon and 33 per cent for those on whom an operation is performed. Patients with peritonitis have a mortality of 85 per cent while those with septicemia have a death rate of 77 per cent.

J. P. GREENHILL.

Gidalewitsch, N. A.: *The Puerperium After Plural Births.* Monatschr. f. Geburtsh. u. Gynäk. 84: 261, 1930.

The puerperium in cases of plural births is entirely different from that in cases of birth of single children because the former frequently is abnormal. Women who have plural births have febrile complications three times as frequently as those who give birth to single babies. The mortality in the former group is ten times as great as in the latter. There appears to be no difference in premature labors and those at term in women who have multiple births. In these women the frequency of operative deliveries is greater than in the case of single births and the morbidity following these operations is twice as great as in the cases without operative interference. Subinvolution of the uterus is common after plural births.

J. P. GREENHILL.

Claye, A. M.: *The Puerperal Morbidity Rate in Patients Delivered Normally.* Brit. M. J. 2: 90, 1929.

The writer investigated 1546 consecutive normal cases delivered in the Leeds Maternity Hospital. The object was to determine whether patients examined vaginally had a higher morbidity rate than those not so examined.

The cases are divided into three classes: (1) Morbid, where temperature exceeded 99° on two or more successive days; (2) Submorbid, where the temperature reached 99° or more at least twice during the first 21 days of the puerperium; (3) Normal, where temperature never reached 99° or reached this mark only once in the 21 days. Temperature was taken in the axilla in all cases.

Findings are as follows: (1) *Vaginally examined*: (a) morbid 2.3 per cent, (b) submorbid 6.8 per cent. Total 9.1 per cent.

(2) *Not vaginally examined*: (a) morbid 1.3 per cent, (b) submorbid 5.3 per cent. Total 6.6 per cent.

(3) *Cases with perineal tears*: (a) morbid 2.6 per cent, (b) submorbid 10.9 per cent. Total 13.5 per cent.

(4) *Other operative procedures*: (a) morbid 10.6 per cent, (b) submorbid not given.

Vaginal examinations were done only after the vulva had been shaved and external parts cleaned with 1 to 1,000 biniodide solution. The examiner wore gloves steeped in biniodide solution after being boiled.

The writer would examine vaginally only cases of antepartum hemorrhage where placenta previa is suspected; cases where degree of dilatation of cervix cannot be ascertained by rectum, usually breech presentations; cases where there seems to be something interfering with the normal progress of labor that cannot be determined by rectal and abdominal examination, and finally when operative procedures such as the application of forceps or the extraction of a breech are about to be instituted.

GEORGE E. HUDSON.

White: *Puerperal and Abortion Sepsis.* Med. J. Australia, 2: 38, 1927.

The paper is based on a study of 70 patients suffering from puerperal and 285 suffering from abortion sepsis. Cultures were obtained from the uterine cavity with an apparatus consisting of an outer glass tube in which was inserted an inner tube, and within this inner tube was placed a woolen swab mounted on a platinum wire. The outer tube was inserted beyond the internal os. The inner tube was then pushed further in and the swab inserted still further to obtain a specimen. The withdrawal took place in the reverse order.

Streptococci were found both within and without the uterus in 45 per cent of the cases, gonococci in 9 per cent, *Staphylococcus aureus* in two cases, coliform bacilli in two cases and *Bacillus Welchii* in one case. In two cases gonococci were found inside the uterus but not on the cervix.

In the acute blood infections *Streptococcus hemolyticus* was almost a constant finding occurring in 85 per cent of cases. The writer feels that nonhemolytic streptococci are commonly present in the genital tract and may cause puerperal sepsis. He feels that this type is undoubtedly an endogenous infection, and that severe puerperal sepsis is mainly caused by hemolytic streptococci which are seldom found in the vaginal flora.

In accounting for this endogenous infection the writer suggests the following methods of contamination: (1) In cases of chronic gonorrhea streptococci often appear as a secondary infection. (2) In multiparae with previous lacerations and erosion of the cervix there is commonly a leucorrhea due to streptococci. (3) Coitus late in pregnancy may be a cause. (4) The mutation of Rosenow in that nonhemolytic streptococci which appear to be a part of the normal vaginal flora may transform under suitable environment into a virulent hemolytic variety.

In considering treatment the writer mentions the use of vaccines, sera, blood transfusions and blood chemical therapy. Under the latter head he describes his technic and results from the use of mereurochrome intravenously and feels that it has given valuable and definite help in septicemia but that it should be used cautiously in cases of nephritis and enterocolitis.

MILLER.

Allan, R. Marshall, and Bryce, Lucy M.: Epidemic of Septic Infection Occurring in a Maternity Hospital. Med. J. Australia 1: 390, 1928.

After the authors had made an investigation for the foci of infection for four septicemia cases in a maternity hospital with one maternal and two infant deaths, they decided a nurse with an infected antrum was the carrier.

The maternal infection became serious on the fourteenth postpartum day, resulting in death on the fifty-fourth day from pyemia. Two babies delivered by different doctors on the forty-sixth and fiftieth days of the maternal infection succumbed. The third baby delivered on the forty-sixth day recovered.

An atypical form of the *Streptococcus mucosus* was isolated from the mother and from one baby, the only two cases cultured. The only similar organism isolated from all the possible carriers was in the culture taken from an antrum of one nurse.

Following the immediate discharge of this nurse no other patient had infections, and because of this the writers are further convinced of their original findings.

H. C. HESSELTINE.

Robinson, A. L. and Cuttle, G. E.: Infectious Puerperal Fever. Lancet 1: 67, 1930.

Following the appearance of scarlet fever in a puerperal patient 8 mothers and 15 babies developed infections. Among the mothers there were two breast abscesses, two septicemias, three scarlet rashes, and one unexplained pyrexia. In the babies eight scarlet rashes (some typical of scarlet fever), six ophthalmiae infections, and one unexplained pyrexia occurred. One mother and one baby died.

Even though the authors consider many puerperal infections due to direct contact they believe that in this series the source was from air borne organisms. The air borne possibility would explain the less likelihood of infections in the home

because the patient is more isolated. Such a possibility raises the question of admitting visitors to the maternity wards and the using of overalls, face masks, and sterilized linens.

This article intends not to belittle the idea of contact contamination, but to emphasize the possibility of air borne infections which may gain entrance through extragenital routes, as well as to recommend the isolation of all hospitalized infected puerperal patients in adequately accommodated quarters having a special nursing staff.

H. C. HESSELTINE.

Devraigne, Baize, and Mayer: A Few Cases of Puerperal Scarlet Fever Seen in the Lariboisière Maternity Hospital. Bull. Soc. d'obst. et de gynéc. 18: 377, 1929.

The authors report a series of six cases of puerperal scarlet fever which were observed during two epidemics of scarlet fever at the Lariboisière Maternity. One case occurred after abortion and the other five after full-term labor. In none of the cases was angina present, but in all of them there was an infection of the genitalia from the beginning. The authors believe that in these cases the portal of entry was the genital organs and not the throat. One of the authors contracted scarlet fever from one of the patients who did not have angina but he did have typical angina. All but one of the patients were primiparas. It may be difficult to differentiate scarlet fever from puerperal infection but in favor of scarlatina are the following signs: Marked acceleration of the pulse, vomiting, a characteristic eruption and desquamation. The babies were isolated from the mothers as soon as the diagnosis was made but in not a single instance did a baby contract scarlet fever in spite of the fact that in all the cases the babies nursed until the diagnosis was confirmed.

J. P. GREENHILL.

Brügelmann, C.: Observations on Puerperal Sepsis Especially Concerning the Localization and Frequency of Metastases. Monatschr. f. Geburtsh. u. Gynäk. 76: 404, 1927.

The author studied 300 cases of puerperal sepsis of which 251 followed abortion, and 49 labor. The mortality for this series was 75 per cent, and in 75 per cent of all the cases metastases were present. Sixty per cent of the patients had thrombophlebitis and the mortality for these patients was 70 per cent. There was an average of 1 to 2 metastases per case and these occurred most frequently in the lungs, less frequently in kidneys, skin, musculature, joints and spleen and least of all in the meninges, myocardium, liver, bones, glands, brain, etc. The most frequent organism causing metastases was the anaerobic *Streptococcus putrificus*. Half as frequent as the latter were the hemolytic streptococcus and mixed infections. In 10 per cent of the cases lymphangitis was present and the mortality for these cases was 50 per cent. Metastases were less frequent than in the thrombophlebitis cases and these were especially localized in the joints. The most common organism found was the hemolytic streptococcus. Endocarditis was present in 12 per cent of the cases and all the patients died. The average number of metastases per patient was 3 and these occurred most frequently in the kidneys, caused most often by the aerobic streptococcus and less frequently the hemolytic streptococcus. In 15 per cent of the cases there were mixed forms such as thrombophlebitis plus lymphangitis, lymphangitis plus endocarditis and abscesses in many organs. Here the mortality was 85 per cent. Most of the metastases occurred in lungs, kidneys, and skin.

J. P. GREENHILL.

Burger, P.: Joint Metastasis in Puerperal Infection. *Gynécologie* 26: 331, 1927.

Burger discusses nine cases of joint metastases in puerperal fever. The condition is relatively uncommon. The joints affected are usually the elbow, shoulder, knee and foot, in order named, and the primary lesion is an embolus, arterial or capillary, in the periarticular tissue, or even in the bone near the joint. The condition is not necessarily due to a septic thrombus and may take place in the course of an ordinary septicemia. It represents a serious factor in the prognosis. Four cases developed as a result of definite septicemia, the others during the course of combined pyemia and septicemia. All nine patients died. One case of particular interest was an infection, antepartum in origin, a septicemia as a result of laryngopharyngitis with subsequent pyemia after involvement of the puerperal uterus. *Streptococcus septicemia* is the most important cause and the prognosis is extremely grave. The complication usually occurs early in the course of the disease.

LITTLE.

Saenger, Hans: Puerperal Gangrene in Septic Conditions and Gynergen Medication. *Zentralbl. f. Gynäk.* 53: 586, 1929.

Saenger from an analysis of the literature finds that most of the so-called cases of gangrene following treatment with gynergen and other ergot preparations have had puerperal infections, or vasomotor diseases of various kinds. In only two of the cases analyzed was the dosage greater than normal. In the noninfected animal enormous doses of ergotamin are required to produce gangrene, and the question is raised if ergotamin is the typical vasoconstrictor that it has been held to be. The author believes that without septic infection or neurospastic predisposition, puerperal gangrene will not appear. He believes atony of the uterus postpartum is the chief indication for the use of the drug, and emphasizes that with the first appearance of prodromal symptoms the drug must be stopped.

WILLIAM F. MENGERT.

Weinzierl, E.: Total Gangrene of the Puerperal Uterus. *Arch. f. Gynäk.* 130: 324, 1927.

The author reports the case of a twenty-one year old primipara, who, on the seventeenth day of a septic puerperium, developed symptoms of diffuse and acute pelvic peritonitis. Laparotomy revealed a totally gangrenous uterus which had completely detached itself from the uterine ligaments and supports, and was lying as a definitely separated sequestrum in a serous sac. This had ruptured and just beneath the defect there was a hole in the uterus. Death occurred on the third day following laparotomy. This entire picture followed a long hard labor which was terminated by a forceps delivery. There had been an early rupture of the uterus followed by the use of oxytoxics to stimulate labor pains. The author is of the opinion that if the rupture of the uterus had not occurred, the sequestered uterus might have been spontaneously expelled with a recovery of the patient.

RALPH A. REIS.

Schumacher, P.: Causes of Post-Operative and Puerperal Thrombosis and Embolism. *Arch. f. Gynäk.* 129: 929, 1927.

Cardiovascular disturbances, adiposity, and postoperative pulmonary disease and other conditions favoring a slowing of the circulation were found in 53 per cent of the cases which developed thrombosis of the legs and in over 70 per cent of the cases which developed embolism. Vaginal operations are especially prone to be followed by embolism. Manual separation of the placenta and tamponade of the

uterus also predispose towards embolism and thrombosis. Infection is a factor in 55 per cent. Those patients who are kept in bed longer than normal for any reason are especially apt to develop embolism and thrombosis because of the prolonged circulatory retardation. Postoperative and puerperal patients should be gotten up, therefore, as early as is possible.

RALPH A. REIS.

Beck, H.: Puerperal Endometritis Following a Retrograde Infection Through a Venous Thrombosis. Arch. f. Gynäk. 131: 701, 1928.

The patient was a primipara, who three days after a normal and spontaneous delivery, developed high fever and chills. The following day she had an eclamptic convulsion and died. Autopsy showed a chronic phlebitis of the right ovarian vein which from gross and microscopic appearances apparently dated from early pregnancy. There was a thrombus present at the junction of the ovarian and renal veins which was also of long standing. Following the delivery, this latter increased in size due to the slowing of the circulatory stream, and the infection flared up. The streptococci present in the thrombus became more virulent and, due to the reversal or cessation of the blood stream through this vein, were able to pass backwards, reach the uterus, and set up an acute endometritis.

RALPH A. REIS.

Chalier, J. and Rousset, J.: Puerperal Tetanus. Progrès méd. 43: 565, 1928.

Postpartum tetanus has practically disappeared and we meet now only with postabortal tetanus, most often following criminal abortion. Placental retention favors the development of tetanus, and it may occur in association with other infections which serve to mask the actual picture. Occasionally, however, it occurs quite by itself. In postmortem specimens tetanus bacilli may be found in sections of the affected tissue. The period of incubation varies like in nonpuerperal tetanus. The cases with short incubation are usually overwhelming and early fatal. Spasm and contracture of the muscles in the region of the anterior abdominal wall and in the lumbosacral region and lower limbs are rather characteristic. Acute and chronic forms are noted, the chronic form being the least frequent. The only cases with favorable outcome have been among the chronic cases. The mortality rate in the acute cases is probably around 90 per cent. Serotherapy as ordinarily advised, but with larger doses and especially by the intravenous route should be used.

GOODRICH C. SCHAUFLER.

Woden: What Procedure Should be Adopted for Retention of Products of Conception? Bruxelles méd. 8: 108, 1927.

On the fifth day postpartum the uterine cavity is invaded by bacteria from the vagina. In 38 per cent of cases streptococci are present. Vicarelli has shown that the addition of placental extract to a bacterial culture greatly enhances growth. Again Warnekros has proved that when the uteroplacental circulation remains intact, organisms of the placental zone penetrate directly into the veins and lymphatics of the uterine wall and thence into the maternal circulation. Thus retained secundines contribute greatly toward the development of a puerperal infection. For this reason the after-birth should be carefully examined for missing cotyledons, succenturiate lobes or incomplete expulsion of membranes.

When little tissue is retained Woden advocates pituitrin or ergot for the first three days postpartum. By this method the retained membranes are usually expelled on the third day. However, in cases where the retention persists and the temperature is not over 38 or 38.5° C., a curettage should be done. The third to fifth day

postpartum is the most advantageous time to carry out this procedure as the uterus is somewhat contracted and more firm, yet the bacterial invasion from the vagina has not occurred. However, where the temperature has risen above 38.5° C., expectant treatment should be continued.

In all operative deliveries showing evidence of retained cotyledons an immediate manual removal of the retained tissue is advocated by the author. Because the cervix is already dilated for a curettage on third day no anesthesia is necessary. A dull curet is used, and curettage is preceded and followed by a sterile intra-uterine douche.

THEODORE W. ADAMS.

Ryberg, C. M.: Some Experiences Concerning Placental Fragments at Parturition. *Acta obst. et gynec. Scandinav.* 6: 153, 1927.

During the last twenty-five years there were 45 cases of retention of placental tissue after labor at the Lund Clinic. Of this number 28 were delivered in the clinic and 17 were sent to the hospital because of this complication. The incidence of this complication in the hospital was 0.13 per cent.

The most striking thing about the study of the placenta after its expulsion is the difficulty of deciding definitely whether or not a piece of placental tissue has been retained in the uterus. Thus among 64 cases where a note was made after examination of the placenta that placental tissue was retained in the uterus, this notation was found to be correct in only 20 per cent. On the other hand, among the 28 patients delivered at the clinic, the retention was not suspected in 13 instances (46 per cent). In 22 per cent of all the cases the placenta had been removed manually or had been expressed by the Credé maneuver, and in 78 per cent it had been expelled spontaneously.

The most important symptom of placental retention was hemorrhage and this occurred in 47 per cent of the cases. In 55 per cent of the cases, the bleeding began during the first week postpartum, in 36 per cent during the second and third weeks, and in 9 per cent between the thirty-first and sixtieth days. In most cases the bleeding was moderate in amount. The next most prominent symptom was fever, in 70 per cent of the cases. In all the cases but one it began during the first week after labor. The fever disappeared in most of the cases where the placental tissue was expelled spontaneously. The latter occurred in half of the patients delivered in the clinic, but among the 17 sent to the hospital after delivery, only two patients expelled the tissue spontaneously. Not one of the patients who passed the tissue spontaneously died. The total number of deaths was seven (15.6 per cent). The author concludes that where there is only a suspicion of partial placental retention, it is best to wait, but where it is certain that placental tissue has been retained, it is better to remove the retained fragments as soon, as completely and as gently as possible.

J. P. GREENHILL.

Balard, P.: Late Hemorrhages in the Postpartum Period. Clinical and Therapeutic Study Based Upon 50 Bordeaux Cases. *Bull. Soc. d'obst. et de gynéc.* 5: 362, 1930.

Some time ago Couvelaire called attention to hemorrhages which occur in the puerperium and which are not due to retention of placental tissue. The cause in these cases is a severe puerperal infection and Couvelaire advocated radical treatment by hysterectomy. Balard collected 50 cases of late puerperal hemorrhages which occurred in the Bordeaux clinic. The mortality was between 20 and 25 per cent hence the condition is very serious. In 26 cases there was placental retention but in 24 cases there was none. In the latter cases severe puerperal infection was present. Fever occurred in 45 per cent of the cases with placental remains and in 30 per cent of those without placental tissue retention. In both types the uterus was large, soft and tender; in both the time of appearance of the

hemorrhage, of the intensity and recurrence was the same. However, in favor of a diagnosis of placental retention are the following facts: These cases are more frequently preceded by an operative delivery. They occur from the eighth to the fifteenth day after delivery whereas the cases without retention usually occur between the seventh and twelfth day. The lochia are frequently purulent and malodorous and the patients complain of pain in the uterus. To make the diagnosis certain it is necessary to do an intrauterine examination under aseptic precautions.

Among the 26 cases with placental retention 5 died. All the cases were treated by cureage, curettement or tamponade and no hysterectomy was performed. Among the 24 cases without retention 4 died. Among those cured, 9 were treated on purely medical lines, 13 by cureage, curettement or tamponade and 2 by hysterectomy. Of the 4 fatal cases, two had had a hysterectomy.

The author strongly advises against tamponade because in 5 of the 9 fatal cases it was employed. It favors retention of the lochia and therefore infection. If a tamponade has been used, the author urges that hysterectomy be performed.

For cases with placental retention the author advocates only digital cureage. If however, the hemorrhage recurs and if fever is present, hysterectomy should be performed and not more than twenty-four or thirty-six hours should be permitted to elapse.

In the cases of hemorrhage without placental retention medical therapy should be used for the mild cases. This consists of hot vaginal douches, sometimes intra-uterine douches, ergot, pituitrin, ice and anti-infection treatment such as sulpharsenol, fixation abscess and transfusion. Hysterectomy should be reserved for the grave cases but one should not delay too long before the operation is done.

J. P. GREENHILL.

Fraenkel, O.: Late Postpartum and Postabortal Hemorrhage. Arch. f. Gynäk. 129: 87, 1927.

Fraenkel does not believe that all cases of delayed postpartum or postabortal hemorrhage are due to the retention of some of the products of conception. He reports a series of 460 such cases of delayed bleeding. Many of these hemorrhages are due to faulty or incomplete involution of the decidua and more especially of the uterine blood vessels. He proves this by sections made from uterine scrapings and from uteri which were removed on account of such delayed and excessive bleeding.

RALPH A. REIS.